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# STAGES, PROGNOSIS AND DURATION OF GLOMERULAR NEPHRITIS IN CHILDHOOD

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Recent studies of glomerular nephritis in childhood, among which may be mentioned those of Guild,[1] Boyd,[2] Aldrich,[3] Blackfan,[4] Levy[5] and Lyttle and Rosenberg,[6] disclose two tendencies of opinion with which our[7] own observations do not permit us to concur. One of these is to regard the prognosis of acute glomerular nephritis in childhood, whether postscarlatinal or not, as almost uniformly good for complete recovery. The other is to regard such other manifestations of renal disease as nephrosis with glomerular episodes (Tappan[8]), chronic nonspecific nephritis (Aldrich[9]), subacute parenchymatous

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1. Guild, H.: The Prognosis of Acute Glomerular Nephritis in Children, Bull. Johns Hopkins Hosp. **48**:193, 1931.

2. Boyd, G. L.: Acute Nephritis in Children, Canad. M. A. J. **17**:894, 1927.

3. Aldrich, C. A.: Clinical Types of Nephritis in Childhood, J. A. M. A. **94**:1637 (May 24) 1930.

4. Blackfan, K.: Acute Nephritis in Children with Special Reference to the Treatment of Uremia, Bull. Johns Hopkins Hosp. **39**:39, 1926.

5. Levy, R.: Die Prognose der akuten diffusen Glomerulonephritis im Kindesalter mit besonderer Berücksichtigung ihres späteren Verlaufs, Jahrb. f. Kinderh. **130**:215, 1931.

6. Lyttle, J. D., and Rosenberg, L.: The Prognosis of Acute Nephritis in Childhood, Am. J. Dis. Child. **38**:1052 (Nov.) 1929.

7. All the material here studied is the result of personal observation by two persons only: by Dr. Thomas Addis up to January 1935, and since then by myself. This fact is stressed as assuring a considerable degree of uniformity in method and comparability of data.

8. Tappan, V.: Prognosis of the Nephrotic Syndrome in Children, Am. J. Dis. Child. **49**:1487 (June) 1935.

9. Aldrich, C. A., and Boyle, H. H.: Chronic Nonspecific Nephritis: Clinical Observations on Forty Children, with Results of Treatment on Full Diets, J. A. M. A. **100**:1979 (June 24) 1933.

nephritis (Holt and McIntosh [10]) and chronic nephritis as entities etiologically unconnected with acute glomerular nephritis.

The idea that acute nephritis may in some instances lead by direct continuity to chronic forms of nephritis and eventually to death from renal failure, which was upheld in pediatric literature as early as 1897 by the elder Holt [11] and was later expressed in greater detail by Addis,[12] has indeed been denied by Guild [1] and by Aldrich,[3] and the opposite view seems today to be generally held by pediatricians.

Until the work of Addis appeared, the theory of Holt and others that acute and chronic (terminal) nephritis are respectively the beginning and the last stages of one continuing process suffered from the lack of conclusive supporting evidence. It was true that albuminuria was not infrequently observed after the acute stage had passed and even persisted for years; likewise a few casts or a few red blood cells were not uncommonly found in the urine (Guild [1]). These abnormalities, often slight or entirely lacking in the results of routine urinalysis, were, however, offset by apparent good health and (when the newer tests became available) by normal excretion of phenolsulfonphthalein and normal levels of nonprotein nitrogen in the blood. They were, in consequence, assumed to be of little or no significance in relation to the patient's general health, to the health of his kidneys or to his prospects of continuing health. The connecting link between acute and chronic nephritis as well as with the renal degenerative phenomena variously known as "tubular nephritis," "parenchymatous nephritis," etc., was supplied by Addis,[12] who, by discovering and applying a suitable quantitative test for pathologic elements in urine, established the existence of a latent stage in nephritis, during which casts, red blood cells, epithelial cells and protein are excreted in abnormally large amounts for periods varying from a month or so up to twenty years or more, thus demonstrating a continuing activity of the renal lesion. During this period the patient remains in apparent good general health, and the ordinary tests for kidney function (excretion of phenolsulfonphthalein, nonprotein blood nitrogen, etc.) indicate that the kidneys are normal. (It is well to recall that these tests continue to give negative results until at least half the kidney is destroyed.) Addis observed that in some cases the latent stage is followed by actual and apparently complete healing. In others he was able to trace a continuously active process through the stages of acute nephritis, latent nephritis, degenerative glomerular nephritis ("nephrosis," etc.) and terminal (chronic)

10. Holt, L. E., Jr., and McIntosh, R.: Holt's Diseases of Infancy and Childhood, ed. 10, New York, D. Appleton-Century Company, 1933.

11. Holt, L. E.: The Diseases of Infancy and Childhood, ed. 1, New York, D. Appleton & Company, 1897.

12. Addis, T.: A Clinical Classification of Bright's Disease, J. A. M. A. **85**: 163 (July 18) 1925.

nephritis to the final episode of uremia. His work, therefore, fully confirmed the observations and inferences of the senior Holt. Since, however, it has dealt mainly (though not exclusively) with adults, it has seemed worth while to us to report the results in a large number of cases of nephritis in childhood studied by the same method.

Three points should be sharply emphasized to clarify the paramount importance of method in the problem and to explain the discrepancies between our conclusions and those of previous writers in the field.

1. Quantitative analysis of suitably concentrated urine is indispensable in determining the diagnosis, classification and prognosis in any case.

2. Studied by the quantitative method and over considerable periods, most of the different manifestations of nephritis in childhood which are commonly regarded as basically different forms of renal disease are found actually to be different stages or phases of one disease, glomerular nephritis.

3. Individual variations in the duration of glomerular nephritis are enormous. It may completely heal in a few weeks or months, or it may persist in latent form many years (twenty or more) during which the existence and potential activity of the lesion can be revealed only by the concentration method. Hence, many nephritic patients pass into adult life and out of the hands of the pediatrician before the disease again becomes clinically manifest. The pediatrician commonly regards these patients as cured.

## CLASSIFICATION

While following the classification of Addis,[12] we omit from consideration here the types which are rare in childhood or have not occurred in our series of children (arteriosclerotic Bright's disease, degeneration from poisoning with heavy metals, malaria, severe jaundice, etc.). Nearly all cases of Bright's disease in childhood fall into two groups, the first of which is numerically small and the second correspondingly large.

1. Pure degenerative Bright's disease ("nephrosis") is characterized by marked proteinuria and cylindruria, often with lowering of the plasma proteins, anasarca and increase in the plasma lipids, but without renal bleeding. The picture of nephrosis, with the single exception of hematuria, is often closely, though temporarily, simulated by the degenerative phase of glomerular nephritis, from which it can be distinguished in many instances only by the concentration test carried out over a considerable period. A careful exclusion of instances of glomerular nephritis leaves those of pure "nephrosis," a rare disease. Differentiation between the two is of great importance, since "nephrosis" is a reversible disorder, subject to spontaneous recovery, and hence, apart from the marked hazard from pneumococcic and some other infections, has a good prognosis, whereas glomerular nephritis in the stage of

degeneration is not a reversible disease and has an extremely grave prognosis. Then too, pure degenerative Bright's disease may have a specific cause, which may be searched for and perhaps removed, thus clearing up the renal lesion.

2. Glomerular Bright's disease is characterized by bleeding from the kidney with varying degrees of proteinuria and cylindruria, in which red blood cells and blood casts constitute the most constant and characteristic of the formed urinary elements. Four stages, or phases, of this disease are to be distinguished:

A. The initial stage follows an acute infection, which may or may not have been noted or remembered, and in its overt and severer form is manifested by gross hematuria, edema, vomiting, headache, hypertension and sometimes severe prostration and convulsions. Oliguria and increase in the value for blood urea are common in this stage.

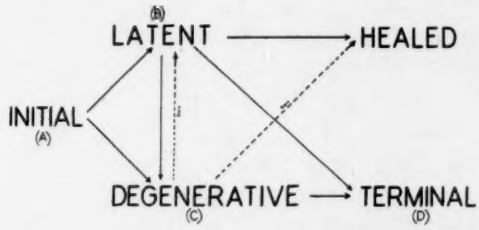


Fig. 1.—Classification of glomerular nephritis according to Addis.

The milder form may be entirely overlooked. The initial stage, whether severe or mild, may terminate in healing or go on to any or all of the later stages.

B. The latent stage, which follows the initial stage, is characterized by the absence of symptoms together with continuing excretion of abnormally large numbers of red blood cells, casts and protein; the excess of these over normal may be slight and usually cannot be detected without use of the concentration method, for reasons that will presently be discussed in more detail. The duration of the latent stage is enormously variable. It may be brief and terminate in complete healing. It may last many years and terminate either in the stage of degeneration or in the terminal stage. In some instances, transient exacerbations occur in the latent stage as the result of intercurrent infection, with visible hematuria. These exacerbations are important since the intercurrent infection or the hematuria may bring the patient to the clinic or private physician, lead to an examination of the urine and so permit the diagnosis of nephritis to be made.

A striking illustration is the case of Grace W. (case 9 in the protocols), a 13 year old Chinese girl, who was first seen in the Stanford Children's Clinic in

1931. In 1932 a routine urinalysis before tonsillectomy revealed moderate albuminuria, and subsequent sediment counts showed the typical changes of latent glomerular nephritis. There was no story of an initial stage, nor had there ever been any symptoms referable to renal disease. A year later tonsillectomy was done, which was not followed by gross urinary changes. Owing to continuing sore throats electrocoagulation of the remaining lymphoid tissue was done at another hospital a few months later, which was immediately followed by marked hematuria. This promptly subsided, but subsequent yearly examinations have shown definite continuation of the renal lesion, and at present only 77 per cent of her functioning renal tissue remains.

Without the concentration tests made before tonsillectomy, one would have concluded from the previous absence of renal symptoms that the glomerular nephritis had begun at the time of gross hematuria; with the tests, there is positive proof that the girl had active, though latent, glomerular nephritis at least a year earlier. If tonsillectomy had not been contemplated, we should have remained in ignorance of the glomerular nephritis, which might not have been discovered until she suddenly became edematous, complained of failing vision or displayed some other striking symptom.

The failure of the ordinary routine urinalyses and of ordinary observation to detect the latent and even the degenerative stage following the initial stage is well shown by the following family history.

Three members of the same family, Walter (4 years), Wendell (5 years) and Eleanor (3 years) had scarlet fever in November 1931. Walter had high fever and was severely prostrated. Twelve days after the onset the urine became grossly bloody and he became edematous. Yearly sediment counts have revealed a continuing active lesion, and he has had bouts of macroscopic hematuria associated successively with pertussis, measles and chickenpox.

Wendell had only a mild attack of scarlet fever and did not go to bed. His physician found albumin in the urine during the convalescence, which disappeared within six months. At no time did the mother note any gross abnormalities of the urine. A concentration test done one year later revealed sediment such as is present in degenerative Bright's disease, with no evidence of hematuria. This has persisted for three years, with no clinical symptoms, the boy growing and developing normally. A sediment count in February 1936 revealed 2,500,000 red blood cells for the first time.

Eleanor also had a mild attack of scarlet fever. Albuminuria was noted during her convalescence and persisted for six months, but no other urinary abnormalities were noted by the doctor or the mother. It was repeatedly suggested that she be brought in for a concentration test, but because of her continuing apparent good health it was not done until August 1935, nearly four years after the initial attack. The sediment count at that time revealed 20,000 casts (33 per cent blood), 12,000,000 red blood cells and 26 mg. of albumin—typical latent glomerular nephritis.

There can be little doubt that Eleanor has had latent glomerular nephritis since 1931, and yet without proper methods of urinary examination we should still be in ignorance of that fact.

The almost universal failure to recognize the latent stage is, in my opinion, chiefly responsible for the divergent opinions on classification of nephritis and for the conflicting statistics on healing and prognosis in general. No patient who has had nephritis can be considered as healed until repeated quantitative studies of concentrated urine have given the kidney a clean bill of health.

C. The degenerative stage [13] is characterized by massive albuminuria and cylindruria, with large numbers of epithelial cells and leukocytes in the urine and a small but still detectable excess of red blood cells. In such cases hypoproteinemia, increased plasma lipids and general anasarca are common, but the last-named condition is by no means invariable. Without the concentration method the increase in red cells on which the correct diagnosis depends is likely to be missed and the case to be set down as one of "nephrosis." Even when it is used, repeated examinations may occasionally be necessary to reveal the presence of erythrocytes.

An added difficulty in the diagnosis of the degenerative stage of glomerular nephritis is the disappearance of red cells from the sediment in some cases. Although this has not been observed in any of the children studied in this series, latent glomerular nephritis in adults with a definite microscopic hematuria has been followed into the degenerative stage, when the red cells disappeared from the sediment, only to reappear as the terminal stage was reached.

Establishment of the presence or absence of hematuria we regard as absolutely vital to prognosis. Without it the differentiation cannot be made between two pathologic entities, one (nephrosis) with a favorable prognosis and the other (degenerative glomerular nephritis) with

13. The nomenclature of the various stages was originally designed to express only the observed clinical facts in terms devoid of any pathologic significance, because at that time the question for investigation was precisely the translation of clinical observations into pathologic facts. For this reason Addis and Oliver (The Renal Lesion in Bright's Disease, New York, Paul B. Hoeber, Inc., 1931) called the disease hemorrhagic Bright's disease. They demonstrated that this disease is in fact glomerular nephritis. In the light of that demonstration there is no longer any reason to use a purely clinical terminology and every advantage is to be gained by calling the disease glomerular nephritis, since this designation has a well established meaning both for clinicians and for pathologists. Similarly, in describing the stage of the disease during which there is clinical evidence of fatty degeneration of the kidney, a high rate of excretion of protein and frequently edema, Addis and Oliver used the term "active stage" until it had been demonstrated by pathologic examination that these signs were actually accompanied by degenerative changes in the glomeruli and tubules of the kidney. Since then, this stage has naturally, and we think justifiably, been called the degenerative stage of glomerular nephritis.

an almost hopeless one. Of the 14 patients in our series with the degenerative syndrome, most of them without a history of an initial stage, 10 have died in uremia, 3 are now progressing toward renal insufficiency and only 1 has recovered. The degenerative stage, therefore, usually, though not always, goes on to the terminal stage (*D*), but we have known this to take as long as fourteen years. In rare instances it may end in healing or revert to the latent stage.

D. The terminal stage is characterized by the various evidences of irreparable renal insufficiency: headache, vomiting, retinal changes, hypertension, azotemia and frequently, though not invariably, acidosis. The urine shows increased amounts of protein, blood and epithelial cells and casts, and the appearance of broad casts is always ominous. The duration of this stage may be as short as two days or as long—even after broad casts have appeared—as four years.

## METHODS OF INVESTIGATION

The general condition, body weight and blood pressure have been carefully followed. Blood urea and, in selected cases, the estimated amount of remaining functioning renal tissue [15] by the urea ratio test have frequently been determined. The principal method on which we have depended and which has been regularly and repeatedly used in all cases is the concentration test of Addis [12] for determining quantitatively the urinary excretion of protein and the composition of the urinary sediment.

The basis of the concentration test is that the formed elements of the sediment—casts and red blood cells especially—are dissolved in a highly dilute or alkaline system but are well preserved in one that is acid and concentrated. The patient goes without fluids during the day preceding the test. In the evening he voids and discards the specimen but carefully notes the time of voiding. The following morning the urine is collected, and the time is again carefully noted. In very young children a shorter period may be used, or specimens may be collected two or more times during the test period. Aliquot portions of the urine are analyzed quantitatively for protein and after centrifugation are examined in the counting chamber to determine the number of casts, red blood cells, leukocytes and epithelial cells. A differential count of the casts is made. The total amount of protein and the total number of formed elements excreted per twelve hours are then computed. Standards of normal twelve hour excretion have been established by

14. Footnote deleted by the author.

15. Addis, T.: Renal Function and the Amount of Functioning Tissue, Arch. Int. Med. **30**:378 (Sept.) 1922. Addis, T., and Watanabe, C. K.: A Method for the Measurement of the Urea-Excreting Function of the Kidneys, J. Biol. Chem. **28**:251, 1916.

Addis [16] for young adults and by Lyttle [17] for children (4 to 12 years) and are shown in table 1.

It is important, at this point, to call attention to certain compelling reasons why the concentration method must be used if the correct diagnosis, nature of the condition and outcome in a given case of renal disease are to be established. I shall cite illustrative examples.

1. Preservation of the formed elements is satisfactory only by this method. We can cite many instances of a routine laboratory examination by the ordinary method in which the specific gravity was low or the reaction alkaline and no casts or red blood cells were found although the patient had active nephritis and with the concentration technic large numbers of casts and red blood cells were demonstrable.

TABLE 1.—*Excretion Per Twelve Hours*

| | Average | Minimum | Maximum | Suggested Upper Normal |
|---|---|---|---|---|
| Addis | | | | |
| Casts | 1,040 | 0 | 4,270 | 5,000 |
| Red blood cells | 65,750 | 0 | 425,000 | 500,000 |
| White and epithelial cells | 822,500 | 32,400 | 1,835,000 | 1,000,000 |
| Protein (albumin), mg. | 30 | ..... | ..... | 30* |
| Lyttle | | | | |
| Casts | 1,085 | 0 | 12,016 | 10,000 |
| Red blood cells | 15,181 | 0 | 129,000 | 600,000 |
| White and epithelial cells | 322,000 | 9,000 | 2,822,000 | 1,000,000 |
| Protein (albumin), mg. | 18.5 | 3 | 47 | 35 |

* On the basis of larger experience this figure will probably be increased to ±60 mg.

Hence, the method is frequently necessary to determine the nature of the renal lesion and, in many instances, the actual existence of a lesion.

Joe M., 8 years old, had latent glomerular nephritis. For five successive weeks he brought to the laboratory specimens of urine which were supposed to be concentrated; in each of these the number of erythrocytes was within normal limits, but the specific gravity was never above 1.014 and the volume was large. Despite vigorous denials by himself and his mother he was suspected of having taken water contrary to instructions. When he was placed in the hospital for a day under strict supervision, fluids were properly restricted and the specimen was found to have a specific gravity of 1.030 and to contain 3,400 casts and 14,000,000 red blood cells per twelve hours. The diagnosis would have been completely missed if dependence had been placed on the previous five specimens.

2. A quantitative determination of the amounts of cells, casts and albumin excreted can be made only by the concentration technic, and, conversely, without it the results of ordinary technic can be extremely

16. Addis, T.: The Number of Formed Elements in the Urinary Sediment of Normal Individuals, J. Clin. Investigation **2**:409, 1926.

17. Lyttle, J. D.: The Addis Sediment Count in Normal Children, J. Clin. Investigation **12**:87, 1933.

misleading. One or two red blood cells per high power field in the ordinary test are commonly regarded as having little significance, but in dilute urine they may indicate an excretion of several million cells per twelve hours—a significant figure. Similarly, a faint trace of albumin in a 1,000 cc. specimen corresponds with about 200 mg. per hundred cubic centimeters, which is definitely pathologic, and in a 100 cc. specimen the same faint trace corresponds with only 20 mg. per hundred cubic centimeters, which is well within normal limits (assuming both to be twelve hour collections), while 200 mg. contained in a 100 cc. specimen gives a "heavy cloud." Since it is almost universal practice to interpret the severity of albuminuria according to the density of the precipitate produced by heat and acetic acid or by a similar test and since this practice is so extremely misleading, we present the data in tabular form for the sake of emphasis. The concentrations of albumin corresponding with the results obtained by the test with heat and acetic acid as commonly reported were supplied by Dr. Harry Wyckoff. The table compares the total values for albumin for like concentrations of albumin in 100 cc. and 1,000 cc. specimens, respectively.

| Albumin | Mg. per Hundred Cc. | 100 Cc., Mg. | 1,000 Cc., Mg. |
|---|---|---|---|
| Faint trace | 20 | 20 | 200 |
| Light cloud | 50 | 50* | 500 |
| Heavy cloud | 100 | 100 | 700 |
| Very heavy cloud | 200+ | 200+ | 2,000+ |

* The underlined figures have pathologic significance for twelve hours or less.

The difficulty of evaluating the significance of albumin in single, untimed specimens is further increased by the great fluctuations in output of albumin that may occur from hour to hour. Twelve hour collection is therefore especially important.

Tommy B. was admitted to the clinic with a history of edema in the past. The routine specimen showed only a faint trace of albumin and an occasional hyaline cast—almost a negligible result. A concentrated specimen, however, showed that 8 Gm. of protein and over 3,000,000 casts were being excreted each twelve hours.

3. The progress of the lesion can be accurately followed only by the concentration method, since no other method affords a reliable comparison of the specimen with another and so permits the increase and decrease of formed elements and of protein excreted to be determined at successive intervals with reasonable accuracy. Variations in dilution and reaction make the ordinary tests nearly worthless for purposes of comparison and of detecting changes for better or for worse in the renal lesions. It follows that the prognosis cannot be determined with any accuracy in most cases by the ordinary tests. Of course, other factors (such as history, blood pressure and level of blood urea) must

be taken into account, but in the main the actual trend of the lesion is best shown by quantitative comparison of successive samples of urine. Examples of these statements will be found in the appended protocols.

4. Finally, attention must be called to the limitations of certain other commonly used tests for renal disease. Normal figures for nonprotein nitrogen (or blood urea) in the blood or for excretion of phenolsulfonphthalein must not be interpreted as excluding nephritis or even serious degrees of nephritis. MacKay and Rytand [18] and Van Slyke and his colleagues [19] have shown that these figures remain well within normal limits until at least half of the normally functioning kidney has been destroyed. The benzidine test for hematuria, used extensively by Aldrich,[3] is undependable for two reasons: first, it is not a sufficiently delicate indicator of the smaller pathologic amounts of blood; second, it will completely fail, even with the large amounts, when the urine is dilute and the red blood cells are hemolyzed. We have made some tests on these points and were unable to obtain positive reactions to benzidine when less than 5,000,000 red cells were added to 120 cc. of unconcentrated urine and the sediment from 10 cc. samples was examined. Moreover, when urine was diluted with a physiologic solution of sodium chloride or with distilled water and 5,000,000 red cells per 120 cc. were added, the tests uniformly gave negative results.

## OBSERVATIONS

We have records [7] of 178 children with glomerular nephritis, all of 15 years or less, who have been in the clinic since 1920. Twenty-four of them could not be followed satisfactorily, and of the remaining 154, 29 have been followed for less than two years. No patient has been considered healed unless he has had a consistently normal reaction to concentration tests for at least one year, and many of the cured patients have been followed for from five to ten years without evidence of recurrence. Many of those whose condition is listed as still active show no clinical evidence of nephritis or of any ill health, but all continue to show pathologic urinary changes revealed by the concentration test. In all cases in which the patient died, the diagnosis of nephritis had been made before death, but in several instances (to be discussed later) death was due to the associated infection, to an intercurrent infection or to some independent cause. Postmortem exami-

18. MacKay, E. M., and Rytand, D. A.: Significance of the Phenolsulphonphthalein Test for Renal Function, Arch. Int. Med. **55**:131 (Jan.) 1935.

19. Van Slyke, D.; McIntosh, F. T.; Moller, E.; Hannon, R. R., and Johnston, C.: Comparison of the Blood Urea Clearance with Certain Other Measures of Renal Function, J. Clin. Investigation **8**:363, 1930.

nation, made in 9 cases, confirmed the diagnosis of glomerular nephritis without exception. The final outcome in 29 of the cases of "still active" lesions in which the patients have had their disease less than two years cannot as yet be determined. Of the 154 patients who could be satisfactorily followed, 57 (37 per cent) are healed, 33 (21.4 per cent) are dead and 64 (41.5 per cent) still have active nephritis, of whom 35 (22.7 per cent) have had the active condition more than two years and will probably not recover. Table 2 gives an analysis of the entire material according to the stage at which the manifestations of the disease were first noted or discovered, showing the state of each patient in 1936.

TABLE 2.—*Summary of the 178 Cases of Glomerular Nephritis in Children Observed in the Stanford Clinic from 1920 to January 1936*

| Stage at Time of Discovery | Present Status | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Healed | Initial Stage | Latent Stage | Degenerative Stage | Terminal Stage | Dead | Not Followed | Total |
| Initial | 44 (40%)* | 1 (1%) | 43 (39%) | 5 (5%) | 3 (3%) | 14 (13%) | 20 | 130 |
| Latent | 5 (40%) | 0 | 3 (27%) | 1 (9%) | 1 (9%) | 1 (9%) | 3 | 14 |
| Degenerative | 1 (7%) | 0 | 1 (7%) | 4 (29%) | 2 (14%) | 6 (42%) | 0 | 14 |
| Terminal | 0 | 0 | 0 | 0 | 0 | 8 (100%) | 0 | 8 |
| Uncertain | 7 (64%) | 0 | 0 | 0 | 0 | 4 (36%) | 1 | 12 |
| Total | 57 (37%) | 1 (0.6%) | 47 (30%) | 10 (6%) | 6 (4%) | 33 (22%) | 24 | 178 |

* Percentages based on number of patients in each group who were followed.

Of the 178 patients, 130 (73.2 per cent) either had a definite history of an initial stage or were actually observed by us in it, and their condition would therefore belong to the type variously known as acute glomerular nephritis, acute hemorrhagic nephritis or acute postinfectious nephritis. One hundred and ten of the patients could be followed by the concentration method, and the outcome was determined up to 1936. Of the 110, only 44 (40 per cent) are now living and healed. Of the 14 who are now dead, in 7 the disease progressed to the degenerative stage, and of these 7, 1 died of pneumococcic peritonitis and in the remaining 6 the condition progressed to the terminal stage and death occurred in uremia, precipitated in 1 case by mumps. Of the remaining 7 who are now dead, 5 died between one and fifteen days after the initial appearance of nephritis, of the original infection or complications (carditis, pneumonia, streptococcic septicemia or meningitis); in these 5 cases the nephritis could be regarded as merely a

contributing factor, although in 2 it was severe enough to be regarded as a major cause of death. In 2 cases death resulted from rheumatic heart disease, and the nephritis was merely incidental (in 1 case it was of minimal grade). If the last 7 patients are deducted from the 110 who could be followed there remain 103 with a known initial stage (acute nephritis), in 7 of whom the nephritis progressed to advanced stages and death occurred, giving a corrected death rate up to the present time of 6.8 per cent, while 44 of the patients are now healed, giving a present recovery rate of 42.7 per cent. The remaining 52 (50.5 per cent) still have active nephritis. While some of these will doubtless recover, 27 of them have had active nephritis for over two years, a period after which healing rarely occurs; moreover, of these 27, 5 are already in the practically hopeless degenerative stage and 3 in the terminal stage. A conservative estimate of the number of deaths from nephritis in the present series when the disease will have run its full course can hardly be less than 34, or 33 per cent, of the 103 patients who survived the original infection; the actual number is likely to be larger.

In all the 14 cases in which the condition was discovered during the latent stage, without any history of acute nephritis and usually without any history of an acute previous infection, it was detected accidentally as the result of the observation of albuminuria, hematuria or casts in a routine urinalysis, usually preoperative. The fact that several of the patients were scheduled for tonsillectomy indicates that previous tonsillar infections had occurred. Abnormalities revealed by the routine test led us to carry out a concentration test and so to discover definite nephritis. Of the 11 patients we have been able to follow, healing has occurred in only 5; in 5 the condition remains active (in 4 cases for more than two years), and in 2 of these it has already entered the degenerative or the terminal stage, while 1 patient has died of renal insufficiency twenty years after the renal lesion was first found on a routine examination. We strongly suspect, because of the accidental nature of the discovery of the condition in these cases and because of the fairly frequent occurrence of small amounts of albumin and other abnormalities in routine analysis, to which little attention is usually paid, that unrecognized latent nephritis is not uncommon.[20]

Of the 14 patients who could be followed and who were seen first when the disease was in the degenerative stage, without history of a preceding initial or latent stage, 6 (42 per cent) are already dead, in 4 the nephritis remains in the same stage, in 2 it has progressed to

20. This problem is now being studied and will be the subject of a future communication.

the terminal stage, in 1 it has reverted to the latent stage and only 1 (7 per cent) has recovered. The prognosis in this group is obviously bad.

Of the 8 patients seen first in the terminal stage without history of previous nephritis, all are dead. The duration of the terminal stage is, however, sometimes surprisingly prolonged. Alice W. had hypertension, increased blood urea and renal failure casts in the urinary sediment for at least four years before death. Mary C. (case 6 in the protocols) lived six years after hypertension and increased blood urea were first noted.

## PROGNOSIS

In assembling and correlating the facts concerning this series an attempt has been made to evaluate the factors on which a prognosis

TABLE 3.—*Relation Between Stage of Nephritis at Time of Discovery ("Onset") and the Outcome; 137 Cases*

| Stage at Time of Discovery | No. of Cases | Present Status | | | | | |
|---|---|---|---|---|---|---|---|
| | | | Condition Still Active | | | | Dead or Condition Active Over 2 Yr. |
| | | Healed | Less than 2 Yr. | Over 2 Yr. | Total | Dead | |
| Initial | 104 | 44 (42%) | 25 (24%) | 27 (26%) | 51 (49%) | 8 (8%) | 35 (34%) |
| Latent | 11 | 5 (45%) | 1 (9%) | 4 (36%) | 5 (45%) | 1 (9%) | 5 (45%) |
| Degenerative | 14 | 1 (7%) | 3 (21%) | 4 (29%) | 7 (50%) | 6 (43%) | 10 (71%) |
| Terminal | 8 | 0 | 0 | 0 | 0 | 8 (100%) | 8 (100%) |

might be based. The following appeared to be of importance: (1) stage at which the disease is first detected, (2) duration of the disease, (3) age of the child when the disease is first detected, (4) hypertension, (5) retention of nonprotein nitrogen in the blood, (6) sex, (7) type of infection preceding the initial stage of the glomerular nephritis and the interval between, (8) intensity of the initial stage and (9) complications.

*Outcome Related to the Stage at Which Disease Was First Detected.*—Table 3 is the tabular résumé of 137 cases in which the outcome is compared to the stage at which the disease was first discovered. Excluded from the series are patients in whom the stage of nephritis when first discovered (called onset for brevity) was uncertain, those who died from the original infection or other causes and not definitely of nephritis and those who could not be adequately followed.

Since, as is shown in table 4, patients whose lesions are known to have remained active for more than two years rarely recover, we

contributing factor, although in 2 it was severe enough to be regarded as a major cause of death. In 2 cases death resulted from rheumatic heart disease, and the nephritis was merely incidental (in 1 case it was of minimal grade). If the last 7 patients are deducted from the 110 who could be followed there remain 103 with a known initial stage (acute nephritis), in 7 of whom the nephritis progressed to advanced stages and death occurred, giving a corrected death rate up to the present time of 6.8 per cent, while 44 of the patients are now healed, giving a present recovery rate of 42.7 per cent. The remaining 52 (50.5 per cent) still have active nephritis. While some of these will doubtless recover, 27 of them have had active nephritis for over two years, a period after which healing rarely occurs; moreover, of these 27, 5 are already in the practically hopeless degenerative stage and 3 in the terminal stage. A conservative estimate of the number of deaths from nephritis in the present series when the disease will have run its full course can hardly be less than 34, or 33 per cent, of the 103 patients who survived the original infection; the actual number is likely to be larger.

In all the 14 cases in which the condition was discovered during the latent stage, without any history of acute nephritis and usually without any history of an acute previous infection, it was detected accidentally as the result of the observation of albuminuria, hematuria or casts in a routine urinalysis, usually preoperative. The fact that several of the patients were scheduled for tonsillectomy indicates that previous tonsillar infections had occurred. Abnormalities revealed by the routine test led us to carry out a concentration test and so to discover definite nephritis. Of the 11 patients we have been able to follow, healing has occurred in only 5; in 5 the condition remains active (in 4 cases for more than two years), and in 2 of these it has already entered the degenerative or the terminal stage, while 1 patient has died of renal insufficiency twenty years after the renal lesion was first found on a routine examination. We strongly suspect, because of the accidental nature of the discovery of the condition in these cases and because of the fairly frequent occurrence of small amounts of albumin and other abnormalities in routine analysis, to which little attention is usually paid, that unrecognized latent nephritis is not uncommon.[20]

Of the 14 patients who could be followed and who were seen first when the disease was in the degenerative stage, without history of a preceding initial or latent stage, 6 (42 per cent) are already dead, in 4 the nephritis remains in the same stage, in 2 it has progressed to

20. This problem is now being studied and will be the subject of a future communication.

the terminal stage, in 1 it has reverted to the latent stage and only 1 (7 per cent) has recovered. The prognosis in this group is obviously bad.

Of the 8 patients seen first in the terminal stage without history of previous nephritis, all are dead. The duration of the terminal stage is, however, sometimes surprisingly prolonged. Alice W. had hypertension, increased blood urea and renal failure casts in the urinary sediment for at least four years before death. Mary C. (case 6 in the protocols) lived six years after hypertension and increased blood urea were first noted.

## PROGNOSIS

In assembling and correlating the facts concerning this series an attempt has been made to evaluate the factors on which a prognosis

TABLE 3.—*Relation Between Stage of Nephritis at Time of Discovery ("Onset") and the Outcome; 137 Cases*

| Stage at Time of Discovery | No. of Cases | Present Status | | | | | |
|---|---|---|---|---|---|---|---|
| | | | Condition Still Active | | | | Dead or Condition Active Over 2 Yr. |
| | | Healed | Less than 2 Yr. | Over 2 Yr. | Total | Dead | |
| Initial | 104 | 44 (42%) | 25 (24%) | 27 (26%) | 51 (49%) | 8 (8%) | 35 (34%) |
| Latent | 11 | 5 (45%) | 1 (9%) | 4 (36%) | 5 (45%) | 1 (9%) | 5 (45%) |
| Degenerative | 14 | 1 (7%) | 3 (21%) | 4 (29%) | 7 (50%) | 6 (43%) | 10 (71%) |
| Terminal | 8 | 0 | 0 | 0 | 0 | 8 (100%) | 8 (100%) |

might be based. The following appeared to be of importance: (1) stage at which the disease is first detected, (2) duration of the disease, (3) age of the child when the disease is first detected, (4) hypertension, (5) retention of nonprotein nitrogen in the blood, (6) sex, (7) type of infection preceding the initial stage of the glomerular nephritis and the interval between, (8) intensity of the initial stage and (9) complications.

*Outcome Related to the Stage at Which Disease Was First Detected.*—Table 3 is the tabular résumé of 137 cases in which the outcome is compared to the stage at which the disease was first discovered. Excluded from the series are patients in whom the stage of nephritis when first discovered (called onset for brevity) was uncertain, those who died from the original infection or other causes and not definitely of nephritis and those who could not be adequately followed.

Since, as is shown in table 4, patients whose lesions are known to have remained active for more than two years rarely recover, we

consider that the combined figure for the dead plus those whose condition has been active for more than two years is the best available index of prognosis. It is clear that the outlook for recovery becomes progressively worse in the successive stages of glomerular nephritis and is hopeless in the terminal stage. The presumptive mortality rate for the initial stage ("acute glomerular nephritis") is much higher than that in other published series, not studied and followed sufficiently long by the concentration test, in which the ensuing latent stage ("still active") was disregarded or overlooked.

*Outcome Related to the Duration of the Disease from the Onset.*—In 131 cases we were able to follow the course of the disease at suffi-

TABLE 4.—*Relation Between Known Duration of Nephritis and the Outcome; 131 Cases*

| | Stage at "Onset" | | | | | |
|---|---|---|---|---|---|---|
| | Initial Stage (98 Cases) | | | Later Stages (33 Cases) | | |
| | Condition | | | Condition | | |
| Known Duration of Disease | Healed | Still Active | Dead | Healed | Still Active | Dead |
| 2 mo. or less | 1 | 3 | 0 | 0 | 0 | 1 |
| 2-6 mo. | 8 | 6 | 0 | 1 | 0 | 2 |
| 6 mo. to 1 yr. | 21 | 10 | 0 | 1 | 0 | 1 |
| 1- 2 yr. | 7 | 6 | 1 | 2 | 4 | 3 |
| 2- 3 yr. | 0 | 4 | 1 | 0 | 1 | 1 |
| 3- 4 yr. | 0 | 4 | 0 | 1* | 1 | 3 |
| 4- 6 yr. | 0 | 5 | 3 | 0 | 1 | 3 |
| 6- 8 yr. | 0 | 6 | 1 | 0 | 2 | 0 |
| 8-10 yr. | 1* | 4 | 0 | 0 | 0 | 0 |
| 10-12 yr. | 0 | 1 | 1 | 0 | 1 | 0 |
| 12-14 yr. | 0 | 2 | 1 | 0 | 1 | 2 |
| 14-16 yr. | 0 | 1 | 0 | 0 | 0 | 0 |
| 20 yr. | 0 | 0 | 0 | 0 | 0 | 1 |
| Under 2 yr. | 37 (59%)† | 25 (40%) | 1 (2%) | 4 (27%) | 4 (27%) | 7 (47%) |
| Over 2 yr. | 1 (3%) | 27 (77%) | 7 (20%) | 1 (6%) | 7 (39%) | 10 (56%) |

* See protocols no. 11 and no. 12.
† The figures in parentheses are percentages of the total number of cases in each of the two groups.

ciently short and regular intervals to tabulate the duration (up to the present time) in relation to the outcome. The results are shown in table 4.

Special attention is called to two facts in this table. First, only 2 patients in the entire series underwent healing of their nephritis when the nephritis had lasted two years or more. Second, the duration of the disease is enormously variable. In 24 cases the disease has lasted more than six years, and in 11, more than ten years.

The infrequency of healing after a duration of more than two years is shown even more clearly in figure 2, a graph of 98 cases in which there was a known initial stage and the patient has been followed up to the present.

*Outcome Related to Age at Which Disease Was First Detected in 138 Cases.*—We prefer this description to the term onset because only in the acute stage can the actual time of onset of the disease be determined with approximate accuracy. In all the later stages the onset has preceded the time of detection by a considerable period, often, we have reason to believe, of several years. For this reason the later stages are more often detected in persons of the older age group, giving an apparent predominance of acute involvement in the younger group and so tending to falsify the statistics.

It appears that while the prognosis for recovery as shown by the group including the dead plus those whose condition has been active

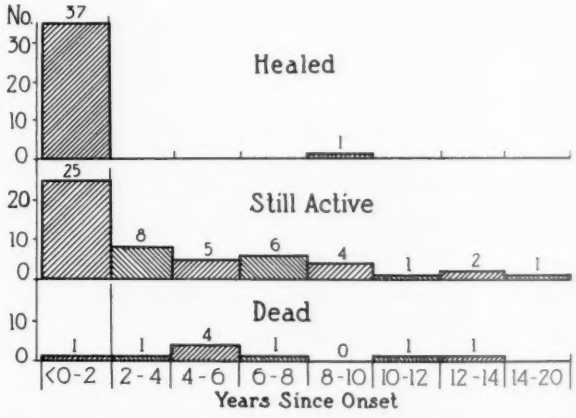


Fig. 2.—Duration related to outcome in 98 cases of glomerular nephritis in which the initial stage was recognized.

for two years or more is somewhat better in the younger age group for those whose condition is recognized in the initial stage, the difference from the older age group is not great, while for those in the later stages the outlook is equally grave at all ages of childhood.

*Outcome Related to Hypertension.*—Hypertension is a feature both of the initial stage and of the terminal stage of glomerular nephritis. Its significance, therefore, must be studied in relation to the chronology of the disease and hence depends on the results of other features of the examination and history. The high systolic and diastolic pressures which are frequently seen during the initial stage drop to normal as the renal lesion heals or goes into latency and therefore have no prognostic significance. It is different with hypertension developing in patients during the latent or degenerative stage, for it is then frequently the first sign of an approaching terminal stage. Persistence of the

hypertension of the initial stage over a period of months is of grave prognostic significance. Our data on blood pressure do not lend themselves readily to tabular presentation.

*Outcome Related to Blood Urea.*—The significance of increases in blood urea (or nonprotein nitrogen) is closely parallel to that of hypertension. During the initial stage it has little prognostic significance, even though it rises to great heights. We have noted 235 mg. of urea per hundred cubic centimeters in the initial stage, followed by recovery. As renal insufficiency develops during the latent and approaching terminal stage, on the other hand, a rise in blood urea becomes ominous. It is not, however, a very early or a delicate indicator, because, as we

TABLE 5.—*Relation Between Age at Which Nephritis Was Discovered and the Outcome; 138 Cases*

| Age and Stage at Time of Discovery | No. of Cases | Present Status | | | | | |
|---|---|---|---|---|---|---|---|
| | | | Condition Still Active | | | | Dead or Condition Active Over 2 Yr. |
| | | Healed | Less than 2 Yr. | Over 2 Yr. | Total | Dead | |
| 1-6 yr. (all stages) | 44 | 15 (33%)* | 16 (36%) | 11 (25%) | 27 (61%) | 2 (4%) | 13 (30%) |
| Initial stage | 39 | 14 (36%) | 15 (38%) | 9 (23%) | 24 (62%) | 1 (2%) | 10 (26%) |
| Later stages | 5 | 1 (20%) | 1 (20%) | 2 (40%) | 3 (60%) | 1 (20%) | 3 (60%) |
| 7-15 yr. (all stages) | 94 | 33 (35%) | 13 (13%) | 23 (24%) | 36 (38%) | 25 (27%) | 48 (51%) |
| Initial stage | 67 | 28 (42%) | 10 (15%) | 17 (25%) | 27 (40%) | 12 (18%) | 29 (43%) |
| Later stages | 27 | 5 (19%) | 3 (11%) | 6 (22%) | 9 (33%) | 13 (48%) | 19 (70%) |

* The figures in parentheses are the percentages of the total number of cases in each group.

have already pointed out, it does not occur until renal damage is far advanced and at least half of the functioning kidney is out of commission.

*Outcome Related to Sex.*—We are unable to find any relation between the sex of the children and the outcome of the disease. In our series the incidence of glomerular nephritis among boys as compared with that among girls is approximately in the ratio of 3:2. With the exception of the group whose condition has been active for more than two years, in which there are equal numbers of boys and girls, the numbers in the group who are healed, whose condition is still active and who are dead maintain the same ratio as the total incidence.

*Outcome Related to the Infection Preceding the Initial Stage.*—Table 5 is an analysis of the records of 73 children whose nephritis

started in a clinically observed initial stage and who have been followed until dead or healed, or whose condition has continued active for more than two years. Children who were observed in the initial stage but whose death could not be attributed directly to the nephritis and also those who have been followed less than two years have been omitted.

TABLE 6.—*Relation Between Sex and the Outcome of Nephritis*

| Sex | No. of Cases | Present Status: Healed | Condition Still Active: Less than 2 Yr. | Condition Still Active: Over 2 Yr. | Condition Still Active: Total | Dead | Dead or Condition Active Over 2 Yr. | Not Followed |
|---|---|---|---|---|---|---|---|---|
| Boys | 94 | 35 (37%)* | 20 (21%) | 19 (20%) | 39 (41%) | 20 (21%) | 39 (41%) | 15 |
| Girls | 60 | 22 (35%) | 9 (15%) | 16 (26%) | 25 (41%) | 13 (21%) | 29 (47%) | 9 |
| Both | 154 | 57 (37%) | 29 (19%) | 35 (22%) | 64 (41%) | 33 (21%) | 68 (43%) | 24 |

* All percentages were calculated for the number of cases followed in each group.

TABLE 7.—*Relation Between the Infection Preceding the Initial Stage of Nephritis and the Outcome; 73 Cases*

| Present Status of Patient | Antecedent Infection | No. of Cases | Interval in Days Between Infection and Ensuing Nephritis: Average | Range |
|---|---|---|---|---|
| Nephritis healed | Scarlet fever | 3 ( 6%) | | |
| | Infections of the upper respiratory tract | 30 (68%) | | |
| | Bronchopneumonia | 1 ( 2%) | | |
| | Infections of skin | 4 (10%) | | |
| | Fever, cause unknown | 2 ( 4%) | | |
| | Total with preceding infection | 40 (90%) | 14.9 | 0-90 |
| | No known infection | 4 (10%) | | |
| Nephritis still active after 2 yr. | Scarlet fever | 5 (21%) | | |
| | Infections of the upper respiratory tract | 12 (50%) | | |
| | Peridental infection | 1 ( 4%) | | |
| | Fever, cause unknown | 4 (17%) | | |
| | Total with preceding infection | 22 (92%) | 19.6 | 1-90 |
| | No known infection | 2 ( 8%) | | |
| Dead from nephritis | Scarlet fever | 2 (40%) | | |
| | Infections of the upper respiratory tract | 3 (60%) | | |
| | Total with preceding infection | 5 (100%) | 20.0 | 1-30 |

The outcome of the nephritis in the 73 children who have been observed since the initial stage has been tabulated according to (*a*) the type of infection preceding the onset of nephritis and (*b*) the interval between the onset of the preceding infection and the appearance of nephritis.

It will be noted that the average interval between infection and ensuing nephritis for those who have recovered is approximately fifteen

days, whereas that for those who are dead or whose condition has been active over two years is about twenty days. The difference does not appear to be statistically significant in view of the small number of cases and the identical range of intervals in all three groups.

As has been noted by all observers, infections of the upper respiratory tract, including tonsillitis, pharyngitis, otitis media and cervical adenitis, are by far the most common infections antecedent to glomerular nephritis. Scarlet fever in our series preceded the nephritis in about 14 per cent of all the cases, and the fact that it occurred in a much higher percentage in the group of patients whose condition is active or who are dead than in those who have recovered is probably of importance.

From our material we cannot conclude that any relationship exists between the intensity of the preceding infection and the outcome of glomerular nephritis. Of course, comparison of the severity of infection can be done only roughly, but the fact that among both the patients who are healed and those in whom the condition is active are patients who had no history of an infection antecedent to the initial stage strongly suggests that the renal lesion progresses irrespective of the intensity of the preceding infection.

*Outcome Related to the Intensity of the Initial Stage.*—We have been unable to find any relationship between the intensity of the initial stage of the glomerular nephritis and the outcome. In our experience children with extreme edema, marked hypertension, severe cerebral manifestations or other grave symptoms have frequently been healed while in others the nephritis has continued to progress slowly or rapidly toward renal insufficiency and death. The many patients whose condition was discovered in the latent, degenerative and terminal stages without history of an initial stage are in our opinion those in whom the initial stage was mild.

*Outcome Related to Complications.*—As is well known, an intercurrent infection in a patient with latent glomerular nephritis may cause an exacerbation. Even slight infections may bring about gross hematuria with increased output of protein and casts, usually without hypertension and edema. In one of our patients intercurrent pneumonia followed by mumps (case 3 in the protocols) caused the nephritis to advance from the latent to the terminal stage, with death after a few days. The increased susceptibility of patients with latent nephritis to recurrent infection of the upper respiratory tract should always make the prognosis more guarded until healing has been established. This

is one of the reasons why the existence of latent nephritis should be known and its progress followed. Rheumatic fever has not been found to be a common complication and was in evidence in only 2 of the 178 cases.

## COMMENT

From the facts shown by this study there can be little doubt that glomerular nephritis in childhood is a much more serious disease than pediatricians currently believe. There can be no question that after the initial attack the renal lesion may persist for many years and that owing to lack of proper appreciation of this possibility and of proper means of examination the continuing Bright's disease will be overlooked.

However, observations by Addis [21] and recently by Lyttle [22] have revealed the interesting possibility that although the prognosis of glomerular nephritis in cases in which the condition has been recognized is necessarily serious, there may be a vast number of instances of subclinical glomerular nephritis in which the condition goes on to healing entirely unnoticed. Lyttle reported in 1933 the occurrence of abnormal amounts of casts, red blood cells and albumin in the urine of 14 of 16 patients who had had scarlet fever from two to eight weeks previously, and in none was there the slightest clinical evidence of nephritis. We are at present following 3 patients with glomerular nephritis which developed after scarlet fever, and the only reason we learned about the renal lesion is that we started doing routine concentration tests on the urine of all patients with scarlet fever. At no time did gross hematuria, hypertension or edema occur, and in 2 cases routine urinalyses were reported as giving negative results. It is possible although not yet proved that similar subclinical glomerular nephritis follows other types of hemolytic streptococcic infections. The subclinical initial stage undoubtedly explains those instances of degenerative and terminal glomerular nephritis in which there is no history of initial nephritis.

From the analysis of our material an eventual fatality of about 40 per cent can be predicted with some confidence. It is, of course, questionable whether this material affords a fair sampling of all glomerular nephritis in children. Attention has been called to the possibility and even the probability that in large numbers of cases mild glomerular nephritis with brief periods of latency followed by complete healing occurs after scarlet fever, streptococcic sore throat and similar conditions. At present, however, such cases are rarely recognized and are

21. Addis, T.: Personal communication to the author.

22. Lyttle, J. D.: The Addis Sediment Count in Scarlet Fever, J. Clin. Investigation **12**:95, 1933.

not taken into account in discussions of prognosis. Therefore our material (with the exception of the 14 cases in which the condition was accidentally discovered) seems to us to be fairly representative of glomerular nephritis in childhood, at least for the region in which our observations were made. As with other diseases in which hemolytic streptococci are involved, the clinical manifestations of glomerular nephritis may show geographic differences. The point requires further study which is now in progress.

We realize that it is difficult to set forth a classification and to discuss the changes that theoretically may occur after the initial stage of glomerular nephritis without having actual cases which may be used as examples. As a substitute for the actual clinical observation of the patient by the reader, we have collected protocols of representative cases illustrating the various stages and transitions of glomerular neph-

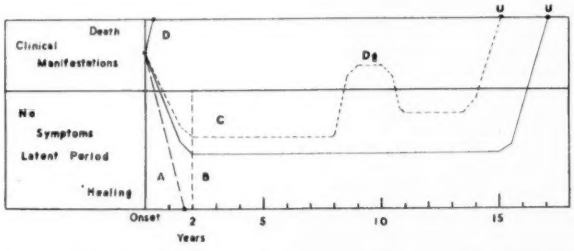


Fig. 3.—Course of glomerular nephritis in cases in which clinical manifestations were present at the onset. *A* represents a case in which the clinically manifest stage was followed by recovery. The vertical broken line at two years indicates the period beyond which healing rarely occurs. *B* represents a case in which a clinically manifest stage was followed by a long period of latency and death in uremia (*U*). *C* represents a case in which a clinically manifest initial stage was followed by a period of latency, a degenerative stage (*Dg*), a stage of latency with more severe urinary abnormalities than were shown before and a terminal stage with uremia (*U*). *D* represents a case in which there were a clinically manifest initial stage and rapidly ensuing death.

ritis in children. We have also made schematic representations of the various possible courses that may follow the initial stage, with particular attention to the relationship of the urinary changes to the clinical manifestations (figs. 3, 4, 5 and 6).

Satisfactory pictures are not generally available of the urinary sediment in the various stages of glomerular nephritis. For this reason, photomicrographs (figs. 7, 8, 9 and 10) are given, showing typical elements of the sediment in the initial, latent, degenerative and terminal stages

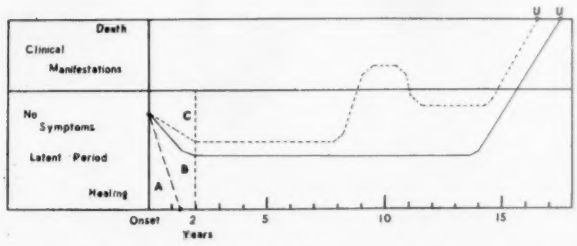


Fig. 4.—Course of glomerular nephritis without clinical manifestations at the onset. *A* represents a case in which a subclinical initial stage was followed by complete healing. *B* represents a case in which a subclinical initial stage and a prolonged latent stage were followed ultimately by death in uremia (*U*). *C* represents a case in which there were a subclinical initial stage, a period of latency, a degenerative stage (*Dg*), a second latent stage and death in uremia (*U*).

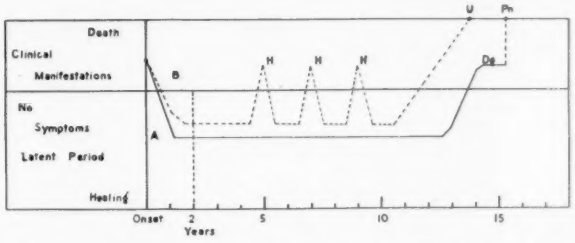


Fig. 5.—Course of glomerular nephritis with clinical manifestations at the onset. *A* represents a case in which clinical manifestations were followed by a long period of latency, a degenerative stage (*Dg*) with a nephrotic syndrome and death from an intercurrent pneumococcic infection (*Pn*). *B* represents a case in which there was a clinically manifest initial stage followed by a latent stage with episodes of gross hematuria (*H*) from intercurrent infection and death in uremia (*U*).

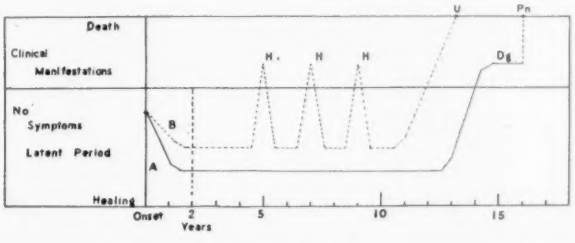


Fig. 6.—Course of glomerular nephritis without clinical manifestations at the onset. *A* represents a case in which there was a subclinical initial stage followed by a long period of latency, a degenerative stage (*Dg*) with a nephrotic syndrome and death from an intercurrent pneumococcic infection (*Pn*). *B* represents a case in which a subclinical initial stage was followed by a latent stage with episodes of gross hematuria (*H*) from intercurrent infection and death in uremia (*U*).

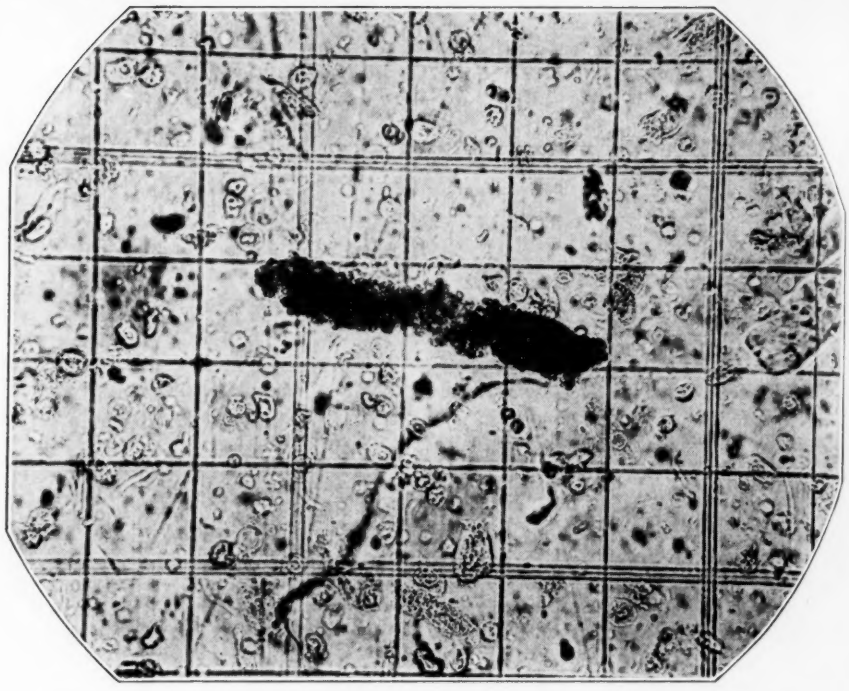

Fig. 7.—Urinary sediment in the initial stage; × 275. The sediment was photographed on an ordinary hemacytometer and shows typical blood casts, many red blood cells and white and epithelial cells. It should be stressed that the blood casts are to a great extent yellow granular casts and it is infrequently that actual red blood cells can be made out in the them.

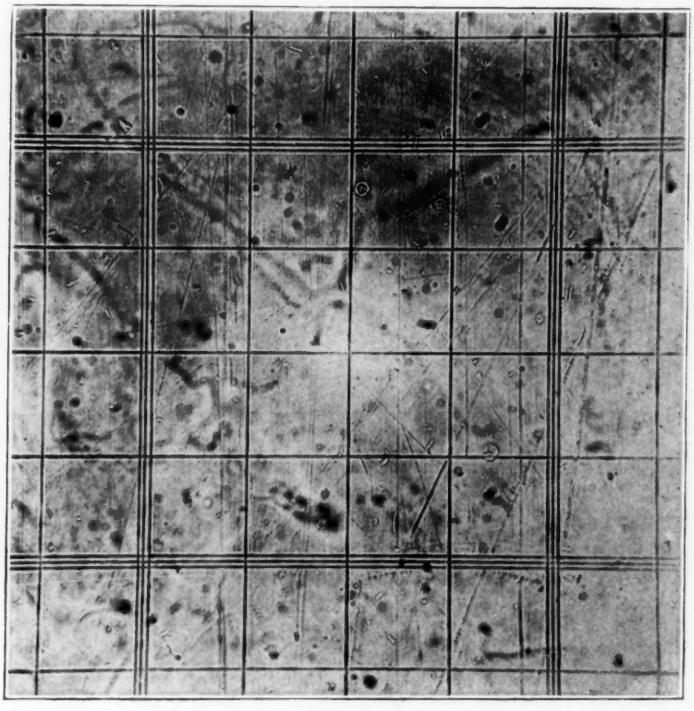

Fig. 8.—Urinary sediment in the latent stage; × 275. The low number of formed elements is striking, but a quantitative analysis of the twelve hour excretion of urine revealed pathologic hematuria.

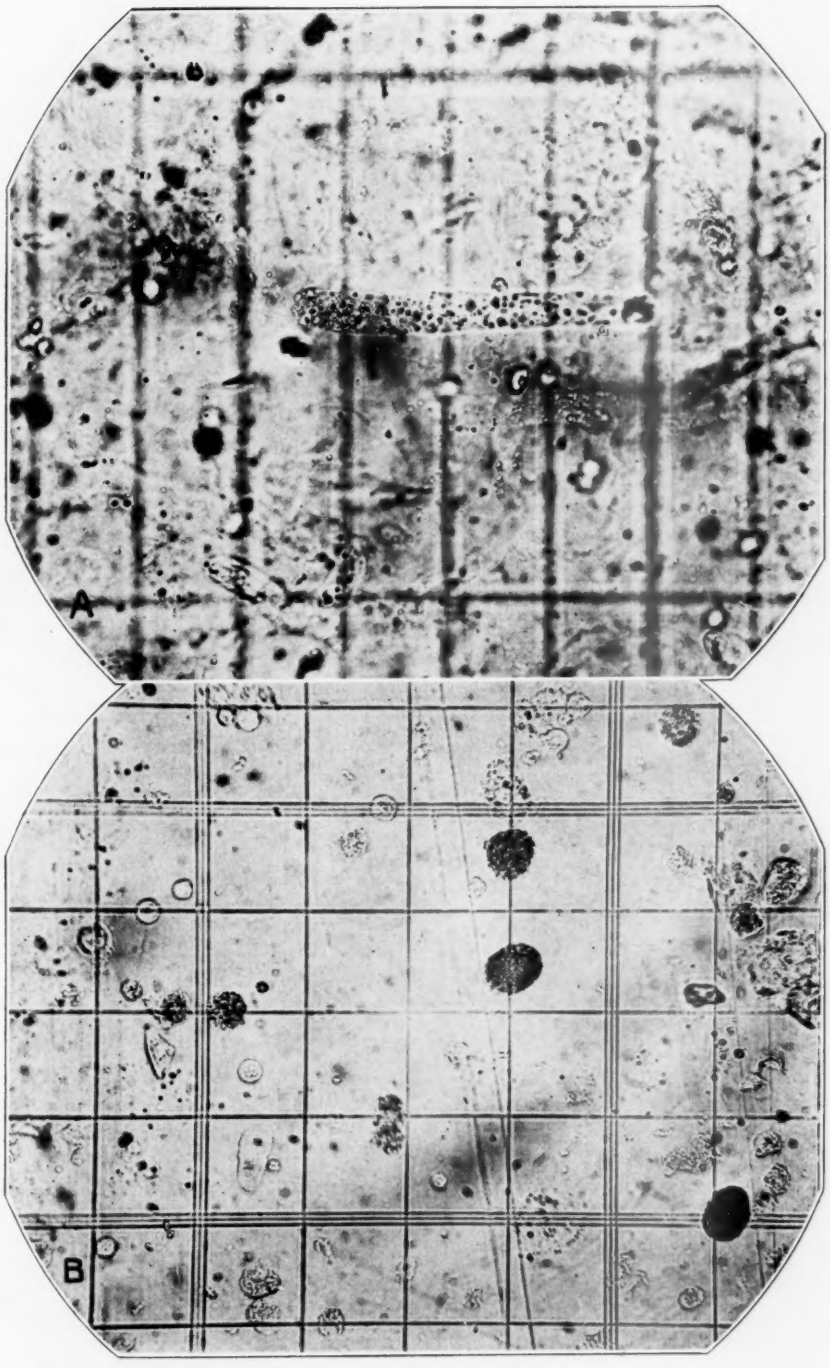


Fig. 9.—*A*, urinary sediment in the degenerative stage; × 275. The photomicrograph shows a hyaline cast with fat droplets obtained from a patient with marked renal degeneration superimposed on the glomerular nephritis. *B*, urinary sediment in the degenerative stage; × 275. The oval fat bodies are found in the urine of patients with intense renal degeneration.

Fig. 10.—*A*, urinary sediment in the terminal stage; × 90. Huge waxy renal failure casts obtained from a patient with terminal nephritis. This type of cast is much wider than the ordinary hyaline or granular cast, as can be shown by comparing the width with that of the hyaline and blood casts which have three times the magnification. *B*, urinary sediment in the terminal stage; × 275. Granular renal failure (broad) cast from a patient with terminal glomerular nephritis. Note the extremely pale, large red blood cells, or shadow cells, as well as the extreme width of the cast.

## CONCLUSIONS

The existence and the persistence of latent glomerular nephritis in childhood, as in adult life can, and in fact usually does, escape detection when quantitative examination of properly concentrated urine is not made. Failure to employ this method commonly leads to such erroneous conclusions as (1) that the patient has no nephritis, (2) that he has completely recovered from an acute attack, (3) that small amounts of albumin, casts or red blood cells in the urine, when found, are without serious significance, (4) that patients who have had acute hemorrhagic nephritis usually recover completely without residual symptoms and (5) that "chronic" nephritis terminating in uremia is unconnected with acute glomerular nephritis.

Glomerular nephritis commonly, if not invariably, enters a latent stage after the initial stage. The initial stage may be and often is overlooked when gross hematuria or fulminating symptoms are absent. Latent glomerular nephritis may terminate in healing or may pass on to the degenerative stage or to the terminal stage, and its duration is enormously variable. The later stages frequently do not occur till some period of adult life.

Between 1920 and 1936 178 children with glomerular nephritis were studied in the Stanford Children's Clinic, of whom 154 have been followed. Of the 154 children, 57 (37 per cent) are now healed, 33 (21 per cent) are dead and 64 (42 per cent) still have active nephritis.

Of the 64 children with continuing activity, 35 (54 per cent) have been in that stage for more than two years and 6 (10 per cent) for more than ten years. With only 2 exceptions, both slightly doubtful, no instance of nephritis lasting over two years in our series has ended in healing. On the basis of our experience, an eventual fatality rate of 40 per cent for glomerular nephritis is a conservative estimate.

The prognosis for the successive stages of glomerular nephritis—active, latent, degenerative and terminal—is progressively worse, the last named being uniformly fatal.

The age of onset (or detection) has no significant relation to prognosis.

Boys outnumbered girls in our series in a ratio of about 3:2, but sex has no relation to prognosis.

Hypertension and increased amounts of blood urea have similar significance and tend to parallel each other; in the initial stage they have no relation to prognosis, but when they appear in the later stages they supply the first indications that the patient is entering the terminal stage of renal insufficiency. The value for blood urea does not become abnormally high as a general rule until 50 per cent or more of the renal tissue fails to function.

Neither the nature of the infection preceding the initial stage nor the intensity of the initial stage itself has any apparent relation to prognosis.

Glomerular nephritis cannot be proved to be healed until repeated quantitative examinations of concentrated urine over a period of at least one year have been normal.

## REPORT OF TWELVE CASES

CASE 1.—*Initial → Latent → Healed.*—Jean G. was born in 1918 and was 11 years old at the onset of nephritis. The past history was irrelevant. Sore throat and fever occurred on Oct. 1, 1929, and shortly thereafter cervical lymphadenitis developed. Vomiting and edema of the face were noted on October 7. Urinalysis on October 8 showed albumin and blood. After several days of marked prostration she improved rapidly, and she has been well since.

| Date | Casts, 12 Hr. | Type of Casts | Red Blood Cells, 12 Hr. | White and Epithelial Cells, 12 Hr. | Albumin, Mg. | Volume, Cc. | Specific Gravity | Blood Urea | Blood Pressure Systolic | Blood Pressure Diastolic |
|---|---|---|---|---|---|---|---|---|---|---|
| 10/10/29 | 544,000 | 4% blood 86% hyaline 10% broad | 103,000,000 | 182,000,000 | 96 | 76 | 1.019 | 235 | 140 | 85 |
| 11/ 1/29 | 179,000 | 16% blood 72% hyaline | 429,000,000 | 1,760,000,000 | 121 | 258 | 1.021 | ... | ... | .. |
| 11/15/29 | 59,900 | 30% blood 60% hyaline | 34,400,000 | 9,800,000 | 69 | 192 | 1.025 | ... | ... | .. |
| 4/ 5/30 | 17,900 | ..... | 3,200,000 | 5,600,000 | 51 | 201 | 1.034 | ... | ... | .. |
| 9/20/30 | 0 | ..... | 554,000 | ..... | 72 | 198 | 1.034 | ... | ... | .. |
| 8/ 1/31 | 0 | ..... | 88,500 | 260,000 | 13 | 177 | 1.033 | ... | 90 | 70 |
| 8/31/33 | 2,850 | ..... | 0 | 420,000 | 73 | 205 | 1.035 | ... | 110 | 80 |

CASE 2.—*Initial → Latent.*—Norma M. was born in 1921 and was 5 years old at the onset of nephritis. Otitis media developed on June 4, 1926. Gross hematuria occurred on June 16, and blood and albumin were found at that time. She has been symptomatically entirely well up to the present; during the interval four routine laboratory urinalyses have been reported as giving entirely negative results or as showing the slightest possible trace of albumin.

| Date | Casts, 12 Hr. | Type of Casts | Red Blood Cells, 12 Hr. | White and Epithelial Cells, 12 Hr. | Albumin, Mg. | Volume, Cc. | Specific Gravity | Blood Urea | Blood Pressure Systolic | Blood Pressure Diastolic |
|---|---|---|---|---|---|---|---|---|---|---|
| 7/16/26 | + | ..... | +++ | + | + | ... | ..... | 52 | ... | .. |
| 7/24/30 | 2,200 | 100% hyaline | 5,050,000 | 370,000 | 49 | 224 | 1.020 | ... | 90 | 65 |
| 7/30/31 | 36,000 | ..... | 1,580,000 | 595,000 | 16 | ... | ..... | ... | 100 | 80 |
| 12/10/32 | 0 | ..... | 26,000,000 | 400,000 | 39 | 268 | 1.033 | ... | 95 | 65 |
| 2/24/34 | 5,300 | ..... | 6,900,000 | 670,000 | 22 | 238 | 1.032 | ... | 90 | 65 |
| 3/30/35 | 24,800 | 66% blood 33% granular | 12,300,000 | 1,788,000 | 65 | 298 | 1.030 | 28.1 | 100 | 70 |
| 3/12/36 | 0 | ..... | 9,000,000 | 2,000,000 | 40 | 275 | 1.013 | ... | 95 | 60 |

CASE 3.—*Initial → Latent → Terminal.*—Robert C. was born in 1920. His age at the onset of the nephritis was 8½ years. Acute otitis media developed on Jan. 2, 1929. Bilateral myringotomy was done on January 12 and bilateral mastoidectomy on January 24. Urinalysis on February 8 showed red blood casts and red blood cells and a light cloud of albumin. He improved clinically, although in June 1929 he was found to be pale, with some edema over the tibia. By March 1,

1930 he was well and had gained 9 pounds (4.08 Kg.). Lobar pneumonia developed on March 15, 1930, and mumps on March 19. Broad casts were soon found, and he died in uremia a few days later. Autopsy was not done.

| Date | Casts, 12 Hr. | Type of Casts | Red Blood Cells, 12 Hr. | White and Epithelial Cells, 12 Hr. | Albumin, Mg. | Volume, Cc. | Specific Gravity | Blood Urea | Blood Pressure Systolic | Blood Pressure Diastolic |
|---|---|---|---|---|---|---|---|---|---|---|
| 3/14/29 | 165,000 | 100% hyaline | 9,680,000 | 2,640,000 | 99 | 275 | 1.019 | 47.1 | ... | .. |
| 5/ 1/29 | 3,072,000 | 100% epithelial | 15,360,000 | 147,912,000 | 415 | 240 | 1.019 | 124.5 | ... | .. |
| 5/18/29 | 108,800 | 100% hyaline | 1,770,000 | 5,011,000 | 188 | 522 | 1.021 | .... | 115 | 95 |
| 10/19/29 | 43,500 | 5% blood | 30,400,000 | 1,800,000 | 147 | 280 | 1.024 | .... | 110 | 70 |
| 3/ 1/30 | 123,000 | 100% hyaline | 12,500,000 | 3,720,000 | 210 | 388 | 1.023 | .... | 95 | 55 |
| 3/26/30 | 3,070,000 | ..... | 327,000,000 | 640,000,000 | 3,310 | 368 | 1.014 | .... | ... | .. |
| 4/ 1/30 | 633,000 | 10% broad | ..... | 550,000,000 | 4,270 | 543 | 1.015 | 225.0 | ... | .. |
| 4/ 8/30 | 785,000 | 100% broad | 184,000,000 | 425,000,000 | 4,070 | 589 | 1.015 | 241.6 | ... | .. |

CASE 4.—*Initial → Latent → Degenerative.*—Mary W. was born in 1916. Her age at the onset of nephritis was 10 years. The past history was negative. A swollen gland below the right ear, with pain and fever, occurred on July 1, 1926. Her face became swollen on July 7, 1926, and a doctor said that the "kidneys were inflamed." Her face again became swollen on Oct. 8, 1926. Since then she has been symptomatically well except for edema of the face for a month in 1928.

| Date | Casts, 12 Hr. | Type of Casts | Red Blood Cells, 12 Hr. | White and Epithelial Cells, 12 Hr. | Albumin, Mg. | Volume, Cc. | Specific Gravity | Blood Urea | Blood Pressure Systolic | Blood Pressure Diastolic |
|---|---|---|---|---|---|---|---|---|---|---|
| 11/ 2/26 | 8,200 | ..... | 4,420,000 | 3,600,000 | 200 | 231 | 1.018 | 34.7 | 105 | 70 |
| 1/14/30 | 195,000 | 19% blood 75% hyaline | 21,600,000 | 11,700,000 | 2,074 | 450 | 1.026 | .... | 130 | 90 |
| 1/10/31 | 382,000 | 5% blood 95% hyaline | 10,400,000 | ..... | 1,403 | 410 | 1.026 | 24.3 | 120 | 80 |
| 1/10/35 | 680,000 | 100% hyaline | 15,100,000 | 2,500,000 | 2,445 | 617 | 1.018 | 41.3 | 140 | 100 |

CASE 5.—*Initial → Latent → Degenerative → Terminal.*—Jack M. was born in 1916. His age at the onset of nephritis was 10 years. The past history was unimportant. Acute tonsillitis and pharyngitis with fever occurred in February 1926. His face was noted to be swollen occasionally in March 1926, and later his ankles swelled slightly. Urinalysis on May 1, 1926, revealed blood and albumin. Since then he has had occasional attacks of gross hematuria, usually associated with infection, and two attacks of gout occurred in 1924 and two in the spring of 1935. He has felt perfectly well otherwise and is in college at present.

| Date | Casts, 12 Hr. | Type of Casts | Red Blood Cells, 12 Hr. | White and Epithelial Cells, 12 Hr. | Albumin, Mg. | Volume, Cc. | Specific Gravity | Blood Urea | Blood Pressure Systolic | Blood Pressure Diastolic |
|---|---|---|---|---|---|---|---|---|---|---|
| 6/26/26 | 584,000 | 10% blood 80% granular | 113,000,000 | 35,200,000 | 412 | 528 | 1.015 | .... | 125 | 85 |
| 9/30/26 | 121,000 | ..... | 16,200,000 | 7,200,000 | 123 | 375 | 1.014 | 75.1 | 130 | 100 |
| 8/ 9/27 | 190,000 | ..... | 24,000,000 | 6,200,000 | 142 | 428 | 1.013 | 76.0 | 130 | 85 |
| 8/11/28 | 350,000 | Blood casts present | 22,000,000 | 4,600,000 | 252 | 240 | 1.019 | 56.3 | ... | .. |
| 6/18/29 | 0 | ..... | 14,280,000 | 2,040,000 | 321 | 425 | 1.018 | 83.4 | 140 | 85 |
| 7/ 5/30 | 170,000 | 100% hyaline | 68,000,000 | 18,700,000 | 366 | 508 | 1.016 | .... | 120 | 80 |
| 3/14/31 | 250,000 | 100% hyaline | 65,000,000 | 9,600,000 | 378 | 540 | 1.016 | 59.8 | 140 | 100 |
| 10/11/32 | 210,000 | ..... | 104,000,000 | 14,000,000 | 1,633 | 500 | 1.014 | 57.7 | 150 | 110 |
| 9/ 7/33 | 220,000 | ..... | 81,000,000 | 4,000,000 | 1,340 | 620 | 1.014 | 55.7 | 145 | 110 |
| 9/11/34 | 970,000 | ..... | 31,000,000 | 13,000,000 | 1,670 | 504 | 1.015 | 82.3 | 170 | 115 |
| 5/23/35 | 120,000 | ..... | 104,000,000 | 12,000,000 | 1,866 | 720 | 1.011 | 87.6 | 170 | 105 |
| 12/ 5/35 | 0 | ..... | 28,000,000 | 3,500,000 | 2,155 | 700 | 1.009 | 92.5 | ... | .. |

CASE 6.—*Initial → Degenerative → Terminal.*—Mary C. was born in 1912. Her age at the onset of nephritis was 11 years. Rhinitis and malaise occurred for a few days in January 1924. Two weeks later she awoke with a sore throat and fever. The urine the next day was red, and a doctor found evidence of glomerular nephritis at that time. Edema with heavy albuminuria occurred for three weeks in October 1926. Edema developed again in February 1927 and was accompanied by headache, nausea and vomiting. These symptoms persisted in mild degree until 1929. She graduated from high school, married and felt well until March 1934, when clinical signs of renal insufficiency began to develop; she died in uremia a year later. Autopsy revealed typical chronic glomerular nephritis.

| Date | Casts, 12 Hr. | Type of Casts | Red Blood Cells, 12 Hr. | White and Epithelial Cells, 12 Hr. | Albumin, Mg. | Volume, Cc. | Specific Gravity | Blood Urea | Blood Pressure Systolic | Blood Pressure Diastolic |
|---|---|---|---|---|---|---|---|---|---|---|
| Jan. 1924 | +++ | Blood | ++++ | ++++ | +++ | | | | | |
| 8/17/27 | 1,010,000 | ..... | 23,600,000 | 22,500,000 | 2,304 | 128 | 1.028 | 71.0 | 125 | 80 |
| 3/20/28 | 628,000 | 1% blood | 37,000 | 32,500,000 | 4,102 | 440 | 1.023 | 59.0 | 105 | 75 |
| 3/12/29 | 292,000 | 100% hyaline | 9,284,000 | 3,504,000 | 4,731 | 365 | 1.025 | 29.0 | 150 | 90 |
| 8/ 5/30 | 1,220,000 | ..... | 10,800,000 | 16,500,000 | 5,630 | 489 | 1.019 | 44.9 | 135 | 90 |
| 10/20/31 | 2,750,000 | ..... | 66,000,000 | 42,000,000 | 5,250 | 912 | 1.019 | 20.4 | 170 | 120 |
| 10/29/32 | 630,000 | 90% hyaline 10% granular | 31,000,000 | 108,000,000 | 4,698 | 618 | 1.014 | 58.6 | 170 | 120 |
| 5/25/33 | 145,000 | ..... | 15,000,000 | 24,000,000 | 5,740 | 752 | 1.014 | .... | 145 | 100 |
| 5/24/34 | 76,000 | ..... | 20,000,000 | 33,000,000 | 6,530 | 1,134 | 1.012 | 123.5 | ... | .. |
| 10/11/34 | 61,000 | 100% broad | 20,000,000 | 80,000,000 | 6,140 | 910 | 1.012 | 119.4 | 180 | 130 |
| 1/24/35 | ..... | Broad | ..... | ..... | 3,750 | 840 | 1.011 | 105.7 | 220 | 150 |
| 4/25/35 | Death and autopsy | | | | | | | | | |

CASE 7.—*Initial → Degenerative → Terminal.*—Vivian R. was born in 1913. Her age at the onset of nephritis was 9 years. Cough and high fever occurred in October 1922, and shortly thereafter the urine became black. A physician diagnosed the condition as Bright's disease at that time. Gross hematuria frequently returned, usually being associated with infections of the upper respiratory tract. She felt well until the spring of 1935, when she became nervous and nauseated; purpura developed, and she died in uremia in May 1935. No autopsy was done.

| Date | Casts, 12 Hr. | Type of Casts | Red Blood Cells, 12 Hr. | White and Epithelial Cells, 12 Hr. | Albumin, Mg. | Volume, Cc. | Specific Gravity | Blood Urea | Blood Pressure Systolic | Blood Pressure Diastolic |
|---|---|---|---|---|---|---|---|---|---|---|
| 11/30/26 | 68,000 | 50% blood 50% hyaline | 1,670,000,000 | ..... | 432 | 244 | 1.016 | 19.8 | 110 | 80 |
| 2/24/27 | 98,000 | ..... | 1,050,000,000 | 5,800,000 | 182 | 505 | 1.014 | .... | 110 | 75 |
| 12/11/28 | 574,000 | 48% blood 46% hyaline | 860,000,000 | 32,400,000 | 358 | 432 | 1.015 | .... | 110 | 75 |
| 12/28/29 | 43,000 | ..... | 26,300,000 | 2,870,000 | 1,002 | 278 | 1.025 | 29.6 | 115 | 85 |
| 12/27/30 | 77,500 | 5% blood 95% waxy | 122,000,000 | 3,070,000 | 1,684 | 254 | 1.024 | .... | 100 | 70 |
| 11/12/31 | 347,000 | ..... | 53,000,000 | 3,600,000 | 622 | 320 | 1.016 | 52.6 | 120 | 80 |
| 1/12/33 | 43,000 | ..... | 20,000,000 | 260,000 | 348 | 345 | 1.016 | .... | 120 | 90 |
| 5/22/34 | 16,000 | ..... | 200,000,000 | 3,000,000 | 868 | 580 | 1.011 | 165.6 | 120 | 80 |
| 8/ 2/34 | 0 | ..... | 23,000,000 | 20,000,000 | 1,436 | ... | ..... | 146.1 | 130 | 90 |
| 11/24/34 | ..... | ..... | ..... | ..... | 1,572 | 590 | 1.014 | 142.0 | 135 | 95 |
| 4/ 8/35 | 186,000 | 25% broad | 840,000 | 8,400,000 | 1,982 | 840 | 1.010 | 285.9 | 150 | 90 |
| 5/ 3/35 | Death | | | | | | | | | |

CASE 8.—*Degenerative → Latent → Healed.*—Martha S. was born in 1915. Her age when the disease was discovered was 12 years. The past history was negative, with no record of streptococcic infection. Swelling developed around the eyes on Aug. 16, 1927. Marked albuminuria was found five days later, and generalized

anasarca developed on August 28. Bronchitis occurred on November 1 and was associated with a marked increase in edema. The edema disappeared on December 1. She has gradually regained strength and has been symptomatically well since December 1927.

| Date | Casts, 12 Hr. | Type of Casts | Red Blood Cells, 12 Hr. | White and Epithelial Cells, 12 Hr. | Albumin, Mg. | Volume, Cc. | Specific Gravity | Blood Urea | Blood Pressure Systolic | Blood Pressure Diastolic |
|---|---|---|---|---|---|---|---|---|---|---|
| 9/22/27 | 4,820,000 | 99% hyaline | 1,620,000 | 14,100,000 | 4,553 | 152 | 1.044 | 43.4 | 110 | 80 |
| 10/27/27 | 2,950,000 | ..... | 13,800,000 | 20,500,000 | 4,298 | 168 | 1.035 | .... | ... | .. |
| 11/26/27 | 330,000 | ..... | 27,100,000 | 12,000,000 | 3,906 | 224 | 1.029 | .... | ... | .. |
| 1/24/28 | 25,800 | ..... | 930,000 | 1,800,000 | 630 | 155 | 1.034 | .... | 90 | 60 |
| 6/30/28 | 0 | ..... | 240,000 | 330,000 | 39 | 120 | 1.039 | .... | ... | .. |
| 12/14/29 | 0 | ..... | 0 | 225,000 | 54 | 250 | 1.032 | .... | 100 | 65 |

CASE 9.—*Latent → Degenerative.*—Grace W. was born in 1920. Her age when the disease was discovered was 12 years. No history of acute infection was obtained. She was moderately obese, and the basal metabolic rate was found to be —28 per cent in 1931. Thyroid medication was given up to September 1935. A routine urinalysis prior to a proposed tonsillectomy revealed albuminuria in May 1932, and the first sediment count was done on July 14, 1932. Tonsillectomy was done in January 1933, with no gross hematuria immediately thereafter. Otitis media and cervical adenitis developed on May 13, 1933. Electrocoagulation of tonsillar tissue was done shortly thereafter and was accompanied by marked hematuria which lasted for three days. She has been symptomatically well since then, with an Addis ratio done in November 1935 revealing only 77 per cent functioning renal tissue remaining.

| Date | Casts, 12 Hr. | Type of Casts | Red Blood Cells, 12 Hr. | White and Epithelial Cells, 12 Hr. | Albumin, Mg. | Volume, Cc. | Specific Gravity | Blood Urea | Blood Pressure Systolic | Blood Pressure Diastolic |
|---|---|---|---|---|---|---|---|---|---|---|
| 7/14/32 | 0 | ..... | 11,224,000 | ..... | 1,269 | 420 | 1.030 | .... | 120 | 75 |
| 8/ 2/32 | 150,000 | 100% hyaline | 5,100,000 | 1,250,000 | 499 | 517 | 1.013 | .... | ... | .. |
| 4/13/33 | 21,000 | 100% hyaline | 8,700,000 | 640,000 | 808 | 255 | 1.030 | .... | 120 | 90 |
| 4/25/33 | 2,100,000 | ..... | 7,400,000,000 | 230,000,000 | 2,436 | 184 | 1.021 | .... | ... | .. |
| 8/29/34 | 399,000 | 91% hyaline 9% granular | 1,236,000 | 5,896,000 | 518 | 120 | 1.041 | .... | 120 | 80 |
| 1/ 3/35 | 71,000 | ..... | 5,888,000 | 1,024,000 | 1,106 | 256 | 1.031 | .... | 140 | 90 |
| 7/18/35 | 238,000 | 100% hyaline | 4,882,000 | 1,287,000 | 1,812 | 286 | 1.031 | 33.0 | ... | .. |
| 9/ 5/35 | 502,000 | 100% hyaline | 2,147,000 | 339,000 | 2,355 | 227 | 1.030 | .... | ... | .. |
| 1/29/36 | 396,000 | ..... | 6,440,000 | 1,840,000 | 1,457 | 230 | 1.035 | .... | 124 | 76 |

CASE 10.—*Degenerative Stage of Glomerular Nephritis Simulating "Nephrosis."* —Freeman L. was born in 1928. His age at the onset of symptoms was 7 years. No past history of streptococcic infections or of any urinary abnormality was obtained. A cough with fever was diagnosed as pneumonia by a physician in January 1935. Generalized anasarca gradually developed six weeks after the onset of pneumonia. Physical examination on the boy's entrance into the hospital revealed generalized anasarca, pansinusitis and pleurisy, with collection of fluid at the base of the left lung. He did fairly well throughout 1935, with periods of generalized edema alternating with periods when he was entirely free from edema. The value for blood cholesterol ranged from 350 to 450 mg. per hundred cubic centimeters, and the plasma proteins remained consistently below 5 Gm. per hundred cubic centimeters. The periods of high blood urea were associated with edema and oliguria. Red blood cells were consistently absent from the urinary sediment until, as noted in the accompanying table, on Feb. 24, 1936, 9,660,000

red blood cells and red blood casts were found in a nonconcentration test. At that time he had generalized anasarca, and the pleurisy and sinusitis were found to have cleared up completely.

| Date | Casts, 12 Hr. | Type of Casts | Red Blood Cells, 12 Hr. | White and Epithelial Cells, 12 Hr. | Albumin, Mg. | Volume, Cc. | Specific Gravity | Blood Urea | Blood Pressure Systolic | Blood Pressure Diastolic |
|---|---|---|---|---|---|---|---|---|---|---|
| 2/11/35 | 1,253,000 | 100% hyaline | 0 | 7,614,000 | 947 | 188 | 1.022 | 28.5 | 116 | 80 |
| 2/15/35 | ..... | ..... | ..... | ..... | 6,003 | ... | ..... | .... | ... | .. |
| 2/20/35 | 30,000 | 100% hyaline | 270,000 | 2,880,000 | 479 | 180 | 1.024 | .... | 130 | 82 |
| 4/20/35 | 60,000 | 100% hyaline | 60,000 | 1,950,000 | 1,522 | 60 | 1.039 | 28.7 | ... | .. |
| 6/28/35 | 62,900 | 100% hyaline | 81,000 | 2,511,000 | 3,495 | ... | ..... | 141.0 | 134 | 80 |
| 7/ 2/35 | ..... | ..... | ..... | ..... | 3,110 | ... | ..... | 69.0 | ... | .. |
| 8/ 1/35 | 21,000 | 100% hyaline | 147,000 | 1,470,000 | 1,209 | ... | ..... | 19.8 | ... | .. |
| 11/ 1/35 | 1,880,000 | No blood | 0 | 9,900,000 | 3,180 | 94 | 1.028 | 56.0 | 112 | 65 |
| 11/15/35 | 61,000 | ..... | 0 | 7,020,000 | 396 | ... | ..... | .... | ... | .. |
| 2/ 8/36 | 1,900,000 | No blood | 228,000 | 4,560,000 | 3,920 | 152 | 1.020 | .... | 120 | 84 |
| 2/24/36 | 3,059,000 | Blood casts present | 9,660,000 | 9,660,000* | 6,955 | 322 | 1.015 | 40.0 | 124 | 88 |

* 1,000,000 oval fat bodies were also present.

CASE 11.—*Initial→Latent→Healed.*—Edward E. was born in 1915. His age at onset was 8 years. He had tonsillitis and acute mastoiditis in 1919 and frequent colds thereafter, without known urinary abnormalities. A chill and high fever occurred on Dec. 26, 1923; the urine became grossly bloody two days later and remained bloody for six months, after which it cleared up macroscopically. For the next few years he continued to have infections of the upper respiratory tract but no visibly bloody urine until cellulitis of the leg in March 1927 caused gross hematuria. Since then he has felt well. Addis ratios revealed from 82 to 85 per cent of functioning renal tissue in 1928 and 1931 and 100 per cent in 1933 and 1934.

| Date | Casts, 12 Hr. | Type of Casts | Red Blood Cells, 12 Hr. | White and Epithelial Cells, 12 Hr. | Albumin, Mg. | Volume, Cc. | Specific Gravity | Blood Urea | Blood Pressure Systolic | Blood Pressure Diastolic |
|---|---|---|---|---|---|---|---|---|---|---|
| 5/16/24 | 865,000 | 64% blood | 144,000,000 | 39,100,000 | 200 | ... | ..... | .. | 90 | 60 |
| 11/17/25 | 63,000 | 100% hyaline | 22,800,000 | 6,750,000 | 722 | ... | ..... | .. | .. | .. |
| 1/12/26 | 37,700 | 68% blood | 12,000,000 | 2,150,000 | 240 | ... | ..... | .. | 85 | 65 |
| 3/27/27 | 12,000 | 3% blood | 560,000,000 | 64,000,000 | 470 | 128 | 1.030 | .. | .. | .. |
| 1/28/28 | 0 | ..... | 810,000 | 345,000 | 102 | ... | ..... | .. | 80 | 55 |
| 2/ 9/29 | 1,420 | 100% hyaline | 343,000 | 114,000 | 76 | ... | ..... | .. | 105 | 70 |
| 2/15/30 | 0 | ..... | 37,000 | 75,000 | 40 | ... | ..... | .. | 100 | 70 |
| 2/ 7/31 | 11,800 | 100% hyaline | 12,000,000 | 1,100,000 | 346 | ... | ..... | .. | 120 | 60 |
| 12/12/31 | 3,300 | ..... | 11,000,000 | 700,000 | 281 | ... | ..... | .. | .. | .. |
| 8/ 3/32 | 0 | ..... | 1,000,000 | 220,000 | 208 | ... | ..... | .. | .. | .. |
| 12/28/33 | 0 | ..... | 500,000 | 620,000 | 145 | ... | ..... | .. | .. | .. |
| 11/24/34 | 0 | ..... | 135,000 | 405,000 | 54 | ... | ..... | .. | 110 | 80 |
| 5/28/35 | 0 | ..... | 157,000 | 15,000 | 68 | 315 | 1.018 | .. | 110 | 80 |
| 1/ 9/36 | 0 | ..... | 900,000 | 175,000 | 67 | 355 | 1.021 | .. | .. | .. |
| 2/13/36 | 0 | ..... | 0 | 250,000 | 64 | 254 | 1.029 | .. | .. | .. |

CASE 12.—*Latent → Healed.*—William M. was born in 1917. His age when the disease was discovered was 13 years. The past history was unimportant except for alopecia that began in 1923 without known cause and progressed to complete absence of hair within eighteen months. He was observed to be pale and tired in December 1930. Urinalysis in January 1931 revealed red blood cells, albumin and casts. There were no renal symptoms until the summer of 1933, when he

had pneumonia and bloody urine. Since then he has felt well. Addis ratios were made in 1932, 1933, 1934 and in January 1936, all showing from 64 to 68 per cent of functioning renal tissue.

| Date | Casts, 12 Hr. | Type of Casts | Red Blood Cells, 12 Hr. | White and Epithelial Cells, 12 Hr. | Albumin, Mg. | Volume, Cc. | Specific Gravity | Blood Urea | Blood Pressure Systolic | Blood Pressure Diastolic |
|---|---|---|---|---|---|---|---|---|---|---|
| 5/28/31 | 25,500 | 13% blood | 10,000,000 | 3,160,000 | 312 | 277 | 1.028 | .. | 130 | 80 |
| 8/31/31 | 47,000 | 11% blood | 5,100,000 | 1,290,000 | 343 | 238 | 1.026 | .. | 110 | 75 |
| 2/ 2/32 | 3,300 | ..... | 1,800,000 | 600,000 | 268 | 240 | 1.028 | .. | ... | .. |
| 6/17/32 | 19,000 | Blood casts present | 515,000 | 1,200,000 | 299 | 346 | 1.023 | .. | ... | .. |
| 5/23/33 | 5,700 | ..... | 100,000 | 270,000 | 152 | 169 | 1.026 | .. | ... | .. |
| 9/19/33 | 6,500 | ..... | 187,000 | 935,000 | 74 | 292 | 1.025 | .. | ... | .. |
| 5/29/34 | 13,500 | 100% hyaline | 1,040,000 | 520,000 | 119 | 314 | 1.026 | .. | 100 | 65 |
| 12/ 8/34 | 8,700 | ..... | 630,000 | 130,000 | 88 | 197 | 1.034 | .. | ... | .. |
| 5/28/35 | 5,400 | ..... | 0 | 300,000 | 85 | 196 | 1.030 | .. | 125 | 85 |

## COMMENT

Cases 11 and 12 have been classed as instances of recovery although it must be admitted that one cannot be absolutely certain of this at the present time. The excretion of red blood cells has been within normal limits in both cases for over a year, and both boys have been symptomatically well. Neither has acquired hypertension, and, most important of all, the Addis tests for the urea ratio have failed to demonstrate any progressive destruction of renal tissue over the past four years. On the other hand, one must note the continuing high albumin output in both cases and also the fact that both boys have previously had periods of from two to three years in which normal numbers of red blood cells were excreted, followed by recurrences of pathologic hematuria. These two cases again emphasize the difficulty of deciding whether or not nephritis has healed. Although we have classed both as instances of healing, we shall not be certain until we have followed them much longer.

## ABSTRACT OF DISCUSSION

Dr. H. F. Helmholz, Rochester, Minn.: This interesting study reopens the field of so-called acute hemorrhagic nephritis.

I think that pediatricians have been inclined to feel that the prognosis is excellent. Certainly, that has been their experience.

Dr. Snoke said nothing about the removal of foci of infection and the other elements of treatment that are used in these conditions. I imagine that he has all these data at hand but because of the shortness of time was not able to give them. It is interesting that in so careful a study as he has made of the condition the prognosis has turned out so badly, and I think that pediatricians will view with a great deal of interest the follow-up of this work. It behooves them to be on the lookout in the years that follow an attack of acute hemorrhagic nephritis to check up on the so-called excellent results obtained.

Dr. Albert W. Snoke, San Francisco: I am sorry that Dr. Aldrich is not here, for we certainly hold entirely opposite views. It would have been of interest to hear him discuss the paper.

We have a most pessimistic attitude concerning therapy at the present time. In fact, when I started the study and drew these conclusions, Dr. Addis doubted the wisdom of publishing them. He remarked that we are endeavoring to show the pediatricians how they can detect glomerular nephritis in the latent stages when the lesion is still active and that we are presenting no suggestions by which they can help the child. All that we are doing is giving the pediatrician a weapon by which he may make an invalid of his patient. This is perhaps true, but it is important that the physician understand the complete nature of the disease if he is to hope ever to treat it intelligently.

We treat foci of infection, but not because we are satisfied that such foci are the cause of nephritis or that they cause a persistence of the renal lesion. We do know that infections may cause exacerbations of glomerular nephritis and consequently we take all possible steps to prevent such recurrences of infection, by the removal of tonsils, clearing up of sinusitis, etc.

We also endeavor to give the children an adequate protein diet. This is done quantitatively by measuring the amount of protein lost in the urine and giving the children this amount in addition to their metabolic requirements.

# INSENSIBLE PERSPIRATION IN CHILDREN

## III. STATISTICAL CORRELATION OF INSENSIBLE PERSPIRATION AND BASAL METABOLISM

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The fact that the insensible perspiration is altered by those factors which alter the basal metabolism suggested to Benedict and his co-workers that there must be a relationship between the two.[1] Accordingly, Benedict and Root [1a] plotted the hourly insensible loss of weight under certain standard conditions with reference to the observed twenty-four hour heat production in the same persons, and they found a close correlation. This was later confirmed by Johnston and Newburgh,[2] Jores,[3] Heller and Schwarz,[4] Magendantz [5] and Levine and his associates.[6] The last-mentioned authors showed that there is a striking correlation between heat production and insensible perspiration, whether they are measured simultaneously in a respiration chamber or independently by a Sauter balance and in a respiration chamber.

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From the Pediatric Service of Dr. Béla Schick, Mount Sinai Hospital.

1. (*a*) Benedict, F. G., and Root, H. F.: Insensible Perspiration: Its Relation to Human Physiology and Pathology, Arch. Int. Med. **38**:1, (July) 1926. (*b*) Benedict, G. G.: Scandinav. Arch. f. Physiol. **49**:89, 1926. (*c*) Benedict, F. G., and Benedict, C. G.: Perspiratio insensibiles: Ihr Wesen and Ihre Ursachen, Biochem. Ztschr. **186**:278, 1927.

2. Johnston, M. W., and Newburgh, L. H.: J. Clin. Investigation **8**:147, 1930.

3. Jores, A.: Ztschr. f. d. ges. exper. Med. **71**:170, 1930; **77**:734, 1931.

4. Heller, H., and Schwarz, A.: Ztschr. f. d. ges. exper. Med. **71**:416, 1930.

5. Magendantz, H.: Deutsches Arch. f. klin. Med. **173**:44, 1932.

6 (a) Levine, S. Z., and Wilson, J. R.: Respiratory Metabolism in Infancy and in Childhood: Elimination of Water Through Skin and Respiratory Passages, Am. J. Dis. Child. **33**:204 (Feb.) 1927. (*b*) Levine, S. Z.; Wilson, J. R., and Kelly, M.: Insensible Perspiration in Infancy and in Childhood: Its Constancy in Infants Under Standard Conditions and the Effect of Various Physiologic Factors, ibid. **37**:791 (April) 1929; (*c*) Insensible Perspiration in Infancy and in Childhood: Proposed Basal Standards for Infants, ibid. **39**:917 (May) 1930. (*d*) Levine, S. Z., and Marples, E.: Insensible Perspiration in Infancy and in Childhood: Basal Metabolism and Basal Insensible Perspiration of the Normal Infant; Statistical Study of Reliability and of Correlation, ibid. **40**:269 (Aug.) 1930.

Such a correlation is possible because of the constant relationship between the total amount of heat produced and the amount lost by vaporization through the skin and lungs. Soderstrom and DuBois [7] found that the heat eliminated through these channels amounted to from 21 to 28 per cent (average, 24 per cent) of the total loss of heat in their normal subjects and to practically the same proportion in their diseased subjects. Levine and Wilson,[6a] similarly, pointed out that this proportion always approximated 25 per cent of the total loss of heat.

Numerous investigators [8] have shown that the heat thus lost is constant in the same subject from day to day and can be accurately measured by determining the insensible loss of weight (insensible perspiration) with a sensitive balance. According to Levine and his associates, variations from day to day in the insensible perspiration do not exceed 8 per cent. Benedict and Root [1a] suggested that a prediction of the basal metabolism is possible from the measured insensible perspiration and plotted a prediction curve for adults. Similarly, Levine plotted a curve for infants. The value of such prediction curves is apparent, especially for infants and young children, whose cooperation in the determination of their basal metabolism cannot be secured and for whom a respiration chamber is not available.

The purpose of this paper is to supply data on the correlation of the basal metabolism and insensible perspiration of older children, to present a statistical analysis of these data as further evidence of the reliability of such a correlation and to propose a prediction curve which will fill the gap between the one proposed by Levine for infants and that proposed by Benedict for adults.

## METHOD OF STUDY

The apparatus, experimental procedure, sources of error and conditions under which we worked were considered in a previous publication.[9] Our experimental conditions may be briefly summarized as follows: (1) the subject awake but thoroughly relaxed and presenting no fluctuation in temperature during the experiment; (2) the clothing and bedding planned with an eye to having a minimum of hygroscopic material; (3) a small breakfast given at least two and one-half hours before the initial weighing, containing not more than 25 calories per kilogram of body weight and having a fluid content not exceeding from 20 to 40 Gm. per kilogram (since such a meal had previously been proved to exert no stimulating

7. Soderstrom, G. F., and DuBois, E. F.: The Water Elimination Through Skin and Respiratory Passages in Health and Disease, Arch. Int. Med. **19**:931 (May) 1917.

8. Benedict, F. G.: Schweiz. med. Wchnschr. **53**:1101, 1923. Meyer, J.: Rev. franç. de pédiat. **1**:409, 1925. Baumecher, W., and Schonthal, L.: Ztschr. f. Kinderh. **40**:211, 1926. DeRudder: ibid. **45**:404, 1928.

9. Ginandes, G. J., and Topper, A.: Insensible Perspiration in Children: I. Experimental Procedure and the Influence of Certain Factors, Am. J. Dis. Child **52**:528 (Sept.) 1936.

effect after that interval either on the insensible loss of weight or on the basal metabolism); (4) a range in room temperature of from 18 to 25 C., in the absence of visible perspiration, and (5) a range in the relative humidity of from 19 to 74.

The procedure consisted in measuring the insensible perspiration for a period of from two to three hours, by the method of weighings in the Sauter balance previously described.[9] At the completion of the weighings the basal metabolism was tested by the Benedict-Roth apparatus. This apparatus stood close to the weighing bed, the test being performed with the child lying quietly in the weighing bed. In some cases the child was carried from the weighing bed to a metabolism table in the same room and the test was performed there instead of in the bed. Several comparative observations showed that this maneuver, carried out with as little disturbance of the subject as possible, had no influence on the basal metabolic rate. Metabolism tests were always performed in duplicate, the minimal figures being accepted as basal only when the difference between the two readings did not exceed 5 per cent. In several instances the metabolism tests were done before the weighings; in most cases, however, they were done after the weighings. The sequence was found not to affect the results, provided the subject was relaxed and standard basal conditions were observed.

## SUBJECTS STUDIED

The children selected for this study were taken from the general pediatric ward. They had come to the hospital because of an acute illness, but they were not studied until from two to four weeks after admission, at which time they were apparently well and ready for discharge. They have been designated as hospital normal.

One hundred experiments were performed on forty-four children between the ages of 5 and 14 years, twenty-one girls and twenty-three boys. The data obtained from these experiments are shown in table 1. At least two experiments were made on most subjects and as many as four on some. If only one experiment was recorded, the subject had been weighed for several days previously and had been trained for the metabolism test. These data were subjected to a statistical analysis[10] (table 2) to establish the correlation between the two variables—basal metabolism and insensible perspiration.

To control the reliability of our results, fifty-six further observations were made on twenty-seven additional children, from 4 to 15 years of age. Of this group eleven were girls, and sixteen, boys; seven of these children were hospital normal, and the rest were suffering from a chronic disease, such as diabetes, leukemia, exophthalmic goiter or nephrosis. The data for this additional group are shown in table 3. The basal metabolic rate is based on the sitting height.[11]

## ANALYSIS OF RESULTS

The results are graphically presented in the charts.[12] Chart 1 contains a smoothed curve statistically derived, showing the linear correla-

10. Amos Dublin, of the Metropolitan Life Insurance Company, assisted in the statistical analysis.

11. Pirquet, C.: An Outline of the Pirquet System of Nutrition, Philadelphia, W. B. Saunders Company, 1922.

12. One gram of insensible perspiration was made to equal 50 calories of heat per twenty-four hours in the preparation of the charts. This is the same relationship that was found to exist for infants (Levine and others[6]).

TABLE 1.—*The Basal Metabolism and Insensible Perspiration of Forty-Four Hospital Normal Children; One Hundred Observations*

| Case | Sex | No. of Experiment | Age, Years* | Height, Cm. | Sitting Height, Cm. | Weight, Kg. | Insensible Perspiration, Gm. per Hour | Basal Metabolism, Total Calories | Diagnosis on Admission |
|---|---|---|---|---|---|---|---|---|---|
| 1. J. D. | M | 1 | 6 | 117 | 63 | 23.0 | 21.90 | 920 | Acute nephritis |
| | | 2 | .. | ... | .. | .... | 20.80 | 895 | |
| | | 3 | .. | ... | .. | .... | 20.10 | 870 | |
| 2. W. G. | M | 4 | 8 | 123 | 65 | 22.5 | 23.77 | 972 | |
| | | 5 | .. | ... | .. | .... | 22.40 | 957 | Pneumonia |
| | | 6 | .. | ... | .. | .... | 22.78 | 960 | |
| 3. H. G. | F | 7 | 7 | 115 | 66 | 22.5 | 23 76 | 890 | |
| | | 8 | .. | ... | .. | .... | 20.00 | 810 | Deafness |
| | | 9 | .. | ... | .. | .... | 22.57 | 880 | |
| | | 10 | .. | ... | .. | .... | 22.22 | 873 | |
| 4. W. B. | M | 11 | 11 | 136 | 74 | 28.0 | 26.30 | 1,231 | |
| | | 12 | .. | ... | .. | .... | 26.30 | 1,193 | Pneumonia |
| | | 13 | .. | ... | .. | .... | 26.10 | 1,252 | |
| 5. R. A. | F | 14 | 7 | 119 | 64 | 19.0 | 21.23 | 927 | |
| | | 15 | .. | ... | .. | .... | 21.10 | 948 | Infestation with pin worms |
| | | 16 | .. | ... | .. | .... | 20.90 | 936 | |
| 6. G. H. | M | 17 | 5 | 118 | 64 | 21.5 | 21.40 | 1,022 | |
| | | 18 | .. | ... | .. | .... | 21.40 | 1,027 | Pneumonia |
| | | 19 | .. | ... | .. | .... | 20.90 | 984 | |
| | | 20 | | | | | | | |
| 7. T. M. | M | 21 | 6 | 116 | 63 | 19.5 | 22.72 | 984 | Hemophilia |
| | | 22 | .. | ... | .. | .... | 23.07 | 926 | |
| 8. R. H. | M | 23 | 7 | 120 | 64 | 18.0 | 19.00 | 900 | |
| | | 24 | .. | ... | .. | .... | 17.10 | 881 | Asthma |
| | | 25 | .. | ... | .. | .... | 17.00 | 893 | |
| | | 26 | .. | ... | .. | .... | 17.47 | 907 | |
| 9. H. N. | M | 27 | 5 | 112 | 61 | 18.0 | 19.35 | 840 | Pneumonia |
| 10. M. S. | F | 28 | 5 | 109 | 58 | 16 0 | 12 76 | 640 | |
| | | 29 | .. | ... | .. | .... | 12.87 | 629 | Pneumonia |
| 11. A. D. | F | 30 | 6 | 107 | 60 | 16.0 | 18.19 | 789 | |
| | | 31 | .. | ... | .. | .... | 18.36 | 780 | Cystitis |
| 12. A. M. | M | 32 | 6 | 124 | 67 | 20.0 | 18.18 | 760 | Pneumonia |
| 13. T. F. | F | 33 | 5 | 100 | 55 | 15.0 | 15.00 | 620 | |
| | | 34 | .. | ... | .. | .... | 14.00 | 600 | Pneumonia |
| | | 35 | .. | ... | .. | .... | 14.28 | 612 | |
| 14. B. R. | F | 36 | 7 | 117 | 61 | 16.0 | 17.64 | 734 | Pneumonia |
| | | 37 | .. | ... | .. | .... | 17.79 | 728 | |
| 15. R. S. | M | 38 | 8 | 128 | 69 | 23.0 | 22.79 | 923 | Pneumonia |
| | | 39 | .. | ... | .. | .... | 22.80 | 912 | |
| 16. H. R. | F | 40 | 10 | 138 | 72 | 32.0 | 24.74 | 1,152 | Vertigo |
| | | 41 | .. | ... | .. | .... | 24.39 | 1,101 | |
| 17. R. S. | M | 42 | 8 | 124 | 68 | 22.5 | 19.38 | 874 | Catarrhal jaundice |
| | | 43 | .. | ... | .. | .... | 20.45 | 860 | |
| 18. J. L. | M | 44 | 7 | 115 | 67 | 23.0 | 21.68 | 973 | Catarrhal jaundice |
| | | 45 | .. | ... | .. | .... | 19.74 | 974 | |
| 19. W. S. | M | 46 | 6 | 111 | 62 | 18.0 | 20.22 | 907 | Healed eczema |
| | | 47 | .. | ... | .. | .... | 20 22 | 868 | |
| 20. N. R. | M | 48 | 8 | 126 | 68 | 24.0 | 22.64 | 980 | Sinusitis |
| | | 49 | .. | ... | .. | .... | 23.07 | 998 | |
| 21. R. F. | F | 50 | 11 | 144 | 76 | 34.0 | 24.00 | 1,123 | Infection of upper respiratory tract |
| 22. S. T. | M | 51 | 13 | 151 | 77 | 38.0 | 23.10 | 1,200 | Erythema nodosum |
| | | 52 | .. | ... | .. | .... | 22.22 | 1,188 | |
| 23. H. S. | M | 53 | 9 | 130 | 71 | 24.5 | 24.13 | 1,080 | Acute rheumatic fever |
| | | 54 | .. | ... | .. | .... | 24.00 | 1,066 | |
| 24. D. M. | F | 55 | 5 | 103 | 59 | 17.5 | 18.20 | 740 | Infestation with tapeworms |
| | | 56 | .. | ... | .. | .... | 18.40 | 740 | |
| 25. C. S. | M | 57 | 9 | 134 | 74 | 33.0 | 25.42 | 1,098 | Infection of upper respiratory tract |
| 26. S. S. | M | 58 | 6 | 107 | 57 | 17.0 | 18.72 | 734 | Healed eczema |
| | | 59 | .. | ... | . | .... | 19.20 | 712 | |
| 27. M. S. | M | 60 | 8 | 134 | 73 | 28.0 | 21.26 | 1,080 | |
| | | 61 | .. | ... | .. | .... | 21.78 | 1,123 | Acute nephritis |
| | | 62 | .. | ... | .. | .... | 21.90 | 1,145 | |

TABLE 1.—*The Basal Metabolism and Insensible Perspiration of Forty-Four Hospital Normal Children; One Hundred Observations—Continued*

| Case | Sex | No. of Experiment | Age, Years* | Height, Cm. | Sitting Height, Cm. | Weight, Kg. | Insensible Perspiration, Gm. per Hour | Basal Metabolism, Total Colories | Diagnosis on Admission |
|---|---|---|---|---|---|---|---|---|---|
| 28. M. O. | F | 63 | 9 | 137 | 71 | 33.0 | 25.00 | 1,089 | Abdominal pain |
| | | 64 | .. | ... | .. | .... | 24.70 | 1,080 | |
| 29. F. M. | M | 65 | 11 | 140 | 75 | 32.0 | 28.83 | 1,158 | Inguinal hernia (no operation) |
| | | 66 | .. | ... | .. | .... | 27.32 | 1,102 | |
| | | 67 | .. | ... | .. | .... | 27.36 | 1,152 | |
| | | 68 | .. | ... | .. | .... | 28.51 | 1,159 | |
| 30. F. A. | M | 69 | 6 | 102 | 58 | 14.0 | 18.51 | 700 | Pneumonia |
| | | 70 | .. | ... | .. | .... | 17.94 | 675 | |
| 31. I. G. | F | 71 | 5 | 107 | 60 | 15 0 | 21.14 | 829 | Infectious arthritis |
| | | 72 | .. | ... | .. | .... | 20.80 | 810 | |
| 32. P. G. | F | 73 | 6 | 110 | 59 | 18.0 | 19.50 | 766 | Acute rheumatic fever |
| | | 74 | .. | ... | .. | .... | 18.50 | 765 | |
| 33. M. R. | F | 75 | 5 | 107 | 61 | 16.5 | 19.61 | 789 | Pneumonia |
| | | 76 | .. | ... | .. | ...., | 20.68 | 800 | |
| 34. A. V. | M | 77 | 8 | 136 | 71 | 43.0 | 31.00 | 1,255 | Pneumonia; obesity |
| | | 78 | .. | ... | .. | .... | 28.60 | 1,254 | |
| | | 79 | .. | ... | .. | .... | 29.10 | 1,248 | |
| 35. M. T. | F | 80 | 10 | 129 | 70 | 28.0 | 23.30 | 1,056 | |
| | | 81 | .. | ... | .. | .... | 23.10 | 1,086 | Migraine |
| | | 82 | .. | ... | .. | .... | 23.86 | 1,140 | |
| 36. B. G. | F | 83 | 9 | 137 | 71 | 32.0 | 25.20 | 1,095 | Vaginal bleeding |
| | | 84 | .. | ... | .. | .... | 25.72 | 1,080 | |
| | | 85 | .. | ... | .. | .... | 25.86 | 1,072 | |
| | | 86 | .. | 139 | 73 | 35.0 | 27.63 | 1,146 | Ambulatory, after discharge |
| 37. M. S. | F | 87 | 9 | 136 | 74 | 34.0 | 28.90 | 1,180 | Eczema |
| | | 88 | .. | ... | .. | .... | 29.10 | 1,188 | |
| 38. L. S. | M | 89 | 8 | 119 | 67 | 21.0 | 19.40 | 1,000 | Asthma |
| 39. W. L. | F | 90 | 8 | 103 | 56 | 18.0 | 17.44 | 789 | Inactive tuberculosis |
| | | 91 | .. | ... | .. | .... | 17.65 | 768 | |
| 40. G. I. | F | 92 | 5 | 93 | 54 | 15.0 | 16.71 | 681 | Acute nephritis |
| 41. J. A. | F | 93 | 8 | 138 | 74 | 40.0 | 25.10 | 1,120 | Pneumonia |
| | | 94 | .. | ... | .. | .... | 25.78 | 1,140 | |
| 42. E. L. | M | 95 | 5 | 122 | 67 | 21.5 | 18.21 | 988 | Marfan's syndrome |
| | | 96 | .. | ... | .. | .... | 17.70 | 972 | |
| | | 97 | .. | ... | .. | .... | 19.75 | 1,000 | |
| 43. G. O. | F | 98 | 8 | 123 | 66 | 20.5 | 19.34 | 900 | Post-tonsillectomy |
| 44. F. P. | F | 99 | 5 | 90 | 54 | 13.0 | 16.67 | 600 | Catarrhal jaundice |
| | | 100 | .. | ... | .. | .... | 16.24 | 605 | |

* Age on nearest birthday.

tion of the basal metabolism and the insensible loss of weight for the forty-four hospital normal children. The one hundred actual observations are shown as individual scatter points about this smoothed curve. It may be seen that the scatter is good, only eleven points being outside the broken lines which indicates a $\pm$ 15 per cent deviation from the smoothed curve. This deviation may be accepted as being within the limits of experimental error.

From table 2 it may be seen that the coefficient of correlation between the basal metabolism and the insensible perspiration in the series of cases is $0.859 \pm 0.0176$. This evidence of a high degree of positive correlation is substantiated by the statistically derived regression lines which in chart 1 closely approximate the smoothed curve. These results are in striking accord with those of Levine, who in an analysis of sixty-

TABLE 2.—*Correlation of Insensible Perspiration and Basal Metabolism in One Hundred Observations on Forty-Four Hospital Normal Children*

| Insensible Perspiration, Gm. per Hour | Metabolism, Calories per 24 Hours | | | | | | | f-Frequency Insensible Perspiration in Class Units | y-Insensible Perspiration in Class Units of 2 Gm. | f times y | f times $y^2$ | fXy |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 600-699 | 700-799 | 800-899 | 900-999 | 1000-1099 | 1100-1199 | 1200-1299 | | | | | |
| 12-13 | 2 | .. | .. | .. | .. | .. | .. | 2 | —4 | — 8 | 32 | 24 |
| 14-15 | 3 | .. | .. | .. | .. | .. | .. | 3 | —3 | — 9 | 27 | 27 |
| 16-17 | 4 | 4 | 2 | 2 | .. | .. | .. | 12 | —2 | —24 | 48 | 44 |
| 18-19 | .. | 11 | 2 | 4 | 1 | .. | .. | 18 | —1 | —18 | 18 | 23 |
| 20-21 | .. | .. | 8 | 8 | 2 | .. | .. | 18 | 0 | 0 | 0 | 0 |
| 22-23 | .. | .. | 3 | 9 | 3 | 4 | 1 | 20 | 1 | 20 | 20 | 11 |
| 24-25 | .. | .. | .. | .. | 7 | 5 | .. | 12 | 2 | 24 | 48 | 34 |
| 26-27 | .. | .. | .. | .. | 2 | 3 | 2 | 7 | 3 | 21 | 63 | 42 |
| 28-29 | .. | .. | .. | .. | .. | 5 | 2 | 7 | 4 | 28 | 112 | 64 |
| 30-31 | .. | .. | .. | .. | .. | .. | 1 | 1 | 5 | 5 | 25 | 15 |
| F-frequency basal metabolism in class units..... | 9 | 15 | 15 | 23 | 15 | 17 | 6 | 100 = n, or total frequency | | 39 Total fy | 393 Total $fy^2$ | 284 Total fXy |
| X-basal metabolism in class units 100 calories..... | —3 | — 2 | — 1 | 0 | 1 | 2 | 3 | | | | | |
| F times X..... | —27 | —30 | —15 | 0 | 15 | 34 | 18 | —5 = total FX | | | | |
| F times $X^2$..... | 81 | 60 | 15 | 0 | 15 | 68 | 54 | 293 = total $FX^2$ | | | | |
| FXy..... | 75 | 38 | 3 | 0 | 22 | 86 | 60 | 284 = total FXy | | | | |

The arbitrary origin of X = 950 calories per 24 hours; the arbitrary origin of y = 21 Gm. of insensible perspiration per hour

The first moments about these origins are:

$c = -0.05$ class units $= -5$ calories $\quad \bar{x} = 945$ calories

$d = 0.39$ class units $= 0.78$ Gm. $\quad \bar{y} = 21.78$ Gm.

The second moments about these origins are:

$\sigma X^2 = 2.93 - (0.05)^2 = 2.927 \quad \sigma X = 1.711$ class units $= 171.1$ calories

$\sigma y^2 = 3.93 - (0.39)^2 = 3.778 \quad \sigma y = 1.944$ class units $= 3.888$ Gm.

The cross product about the means $= P = 2.84 - (-0.05)(0.39) = 2.859$

$$\text{The coefficient of correlation} = \vee = \frac{P}{\sigma X \sigma y} = \frac{2.859}{3.326} = 0.859 \pm 0.0176$$

$$M_x = \frac{2.859 \times 2 \times 100}{2.927 \times 100 \times 100} = 0.0192$$

$$\text{The probable error (P.E.)} = \frac{0.6745\,(1 - \vee 2)}{\sqrt{100}} = 0.176$$

$$M_y = \frac{2.859 \times 2 \times 100}{3.778 \times 2 \times 2} = 37.837$$

Formulas for regression lines:

For insensible perspiration: $y - 21.78 = 0.0192\,(X - 945)$

$y = 21.876 + 0.0192\,(X - 1000)$

For basal metabolism: $X - 945 = 37.837\,(y - 21.78)$

$X = 915.5 + 37.8\,(y - 20)$

two observations on infants found the coefficient of correlation to be $0.885 \pm 0.018$. In an analysis of a collected series of two hundred similar observations, which included observations on infants, adults and a few older children, he found a coefficient of $0.9417 \pm 0.0064$. When we combined those two hundred observations with our own one hundred actual observations and subjected the entire three hundred to a statistical analysis, we found a coefficient of $0.939 \pm 0.0045$. The high order of correlation in this combined series furnishes additional proof of the consistent relationship between basal metabolism and insensible perspiration in the human subject.

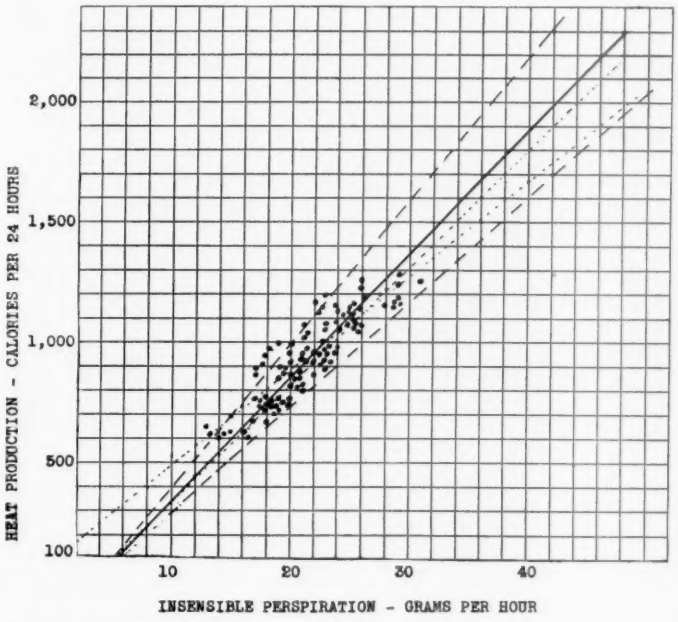


Chart 1.—The relationship of metabolism to insensible perspiration in one hundred observations on forty-four hospital normal children. The individual observations are represented by scatter points. The broken lines indicate a deviation of 15 per cent from the smoothed curve. The dotted lines represent the regression lines computed by statistical methods.

The high degree of correlation of these two variables, as shown for our series of children, makes possible the accurate prediction of the basal metabolism from the insensible loss of weight for the age group studied—an age group hitherto not reported on in the literature. This prediction may be made from the smoothed curve shown in chart 1, which was statistically derived from our data and projected beyond the age group studied.

TABLE 3.—*Basal Metabolism and Insensible Perspiration: Fifty-Six Observations on Twenty-Seven Additional Children (Hospital Normal and Abnormal)*

| Case | Sex | Number of Experiment | Age, Years | Height, Cm. | Sitting Height, Cm. | Weight, Kg. | Insensible Perspiration, Gm. per Hour | Basal Metabolism, Total Calories | Basal Metabolic Rate, Percentage | Diagnosis at Time of Study |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 R. K. | F | 1 | 8 | 124 | 68 | 24.5 | 26.54 | 1,032 | +11 | Anemia due to bleeding from esophageal varices; 4 years after splenectomy |
| | | 2 | .. | ... | .. | .... | 26.40 | 1,080 | +17 | |
| 2 A. S. | F | 3 | 13 | 129 | 70 | 33.0 | 34.42 | 1,711 | +74 | Diabetes with ketosis; blood sugar, 560 mg. |
| 3 E. E. | F | 4 | 8 | 141 | 69 | 33.0 | 28.80 | 1,296 | +36 | Active afebrile primary tuberculosis |
| | | 5 | .. | ... | .. | .... | 27.40 | 1,266 | +33 | |
| | | 6 | .. | ... | .. | .... | 28.00 | 1,248 | +31 | |
| 4 D. M. | F | 7 | 5 | 103 | 59 | 13.0 | 15.00 | 750 | + 9 | Convalescent after severe diarrhea |
| | | 8 | .. | ... | .. | .... | 13.69 | 769 | +10 | |
| 5 R. W. | M | 9 | 5 | 118 | 67 | 22.0 | 15.14 | 727 | −17 | Convalescent after very toxic pneumonia |
| | | 10 | .. | ... | .. | .... | 15.36 | 710 | −19 | |
| 6 A. W. | M | 11 | 14 | 146 | 73 | 31.5 | 24.20 | 1,208 | +13 | Diabetes mellitus (controlled) |
| | | 12 | .. | ... | .. | .... | 24.32 | 1,195 | +11 | |
| | | 13 | .. | ... | .. | .... | 24.17 | 1,147 | + 8 | |
| | | 14 | .. | ... | .. | .... | 19.67 | 1,136 | + 7 | Morning dose of insulin omitted |
| | | 15 | .. | ... | .. | .... | 23.00 | 1,085 | + 2 | |
| | | 16 | .. | ... | .. | .... | 22.88 | 1,091 | + 2 | |
| 7 M. C. | M | 17 | 5 | 101 | 58 | 17.0 | 17.45 | 607 | − 9 | Chronic nephrosis with slight edema |
| | | 18 | .. | ... | .. | .... | 17.40 | 617 | − 8 | |
| 8 D. S. | M | 19 | 4 | 100 | 59 | 20.0 | 15.00 | 608 | −13 | Medulloblastoma |
| | | 20 | .. | ... | .. | .... | 16.00 | 620 | −10 | |
| 9 C. G. | M | 21 | 11 | 156 | 81 | 21.8 | 42.00 | 1,891 | +44 | Exophthalmic goiter |
| 10 L. S. | F | 22 | 15 | 150 | 77 | 34.0 | 30.77 | 1,427 | +20 | Thrombosis of the splenic vein |
| | | 23 | .. | 151 | 78 | 41.0 | 24.60 | 1,243 | + 2 | Convalescent, 5 months after splenectomy |
| 11 F. P. | F | 24 | 5 | 90 | 54 | 13.0 | 12.88 | 563 | − 4 | Hospital normal after catarrhal jaundice |
| 12 P. M. | M | 25 | 13 | 150 | 75 | 38.0 | 33.00 | 1,350 | +20 | Tuberculous cervical adenitis |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 13 | E. L. | M | 26 | 5 | 122 | 67 | 21.5 | 26.47 | 1,140 | +27 | Infection of the upper respiratory tract with a temperature of 101 F. |
| 14 | R. G. | M | 27 | 6 | 111 | 61 | 18.75 | 26.00 | 778 | + 5 | Diabetes insipidus; Legg-Perthe's disease |
| 15 | A. R. | M | 28 | 7 | 126 | 69 | 21.0 | 31.50 | 1,280 | +34 | Acute cervical adenitis, with a temperature of 102 F. |
| 16 | P. G. | F | 29 | 8 | 127 | 69 | 30.0 | 23.07 | 988 | + 4 | Hospital normal after acute pyelitis |
| 17 | L. C. | M | 30 | 13 | 155 | 78 | 38.0 | 39.41 | 1,500 | +23 | Chronic myeloid leukemia |
| | | | 31 | .. | ... | .. | .... | 40.69 | 1,600 | +31 | 1 day after first high voltage roentgen treatment |
| | | | 32 | .. | ... | .. | .... | 33.34 | 1.426 | +17 | 3 days after first high voltage roentgen treatment |
| | | | 33 | .. | ... | .. | .... | 20.50 | 1,171 | — 4 | 1 day after course of 10 high voltage roentgen treatments |
| | | | 34 | .. | ... | .. | .... | 20.41 | 1,158 | — 5 | 2 days after course of 10 high voltage roentgen treatments |
| | | | 35 | .. | 156 | 80 | 38.0 | 26.42 | 1,306 | + 2 | 2 months later, ambulatory |
| 18 | A. E. | M | 36 | 6 | 117 | 62 | 17.5 | 20.23 | 838 | + 9 | Hospital normal after infection of the upper respiratory tract |
| | | | 37 | .. | ... | .. | .... | 19.45 | 786 | + 2 | |
| | | | 38 | .. | ... | .. | .... | 19.67 | 790 | + 2 | |
| | | | 39 | .. | ... | .. | .... | 22.60 | 822 | + 4 | |
| 19 | E. C. | M | 40 | 10 | 129 | 72 | 31.0 | 22.22 | 1,108 | + 7 | Diabetes mellitus (controlled) |
| | | | 41 | .. | ... | .. | .... | 19.28 | 1,123 | + 8 | Morning dose of insulin omitted |
| 20 | M. L. | F | 42 | 11 | 145 | 77 | 34.5 | 20.24 | 1,050 | —13 | Chronic nephrosis with edema |
| | | | 43 | .. | ... | .. | .... | 16.21 | 972 | —20 | |
| | | | 44 | .. | ... | .. | .... | 16.00 | 967 | —21 | |
| | | | 45 | .. | ... | .. | .... | 22.14 | 1,086 | — 9 | Edema not apparent |
| 21 | N. W. | M | 46 | 6 | 120 | 65 | 23.0 | 23.58 | 1,150 | +36 | Chronic malaria |
| 22 | M. L. | F | 47 | 5 | 113 | 63 | 19.0 | 22.00 | 870 | +10 | Hospital normal after pneumonia |
| | | | 48 | .. | ... | .. | .... | 22.23 | 840 | + 6 | |
| 23 | B. J. | M | 49 | 8 | 135 | 73 | 31.0 | 23.69 | 1,166 | + 9 | Hospital normal after pneumonia |
| 24 | B. S. | F | 50 | 7 | 104 | 59 | 13.0 | 20.41 | 815 | +17 | Dermatomyositis |
| | | | 51 | .. | ... | .. | .... | 21.14 | 809 | +15 | |
| 25 | L. S. | F | 52 | 6 | 110 | 61 | 17.0 | 17.64 | 752 | + 1 | Hospital normal after mild cerebrospinal meningitis |
| | | | 53 | .. | ... | .. | .... | 18.05 | 730 | — 2 | |
| 26 | N. S. | M | 54 | 10 | 140 | 75 | 32.0 | 23.08 | 1,200 | + 7 | Hospital normal after pneumonia |
| | | | | | | | | 22.64 | 1,166 | + 4 | |
| 27 | P. L. | M | 55 | 8 | 135 | 74 | 36.0 | 27.91 | 1,290 | +18 | Acute rheumatic fever, with a temperature of 101 F. |
| | | | 56 | .. | ... | .. | .... | 26.48 | 1,296 | +19 | |

* Basal metabolic rate is based on sitting height (Pirquet [11]).

TABLE 4.—*Correlation of Insensible Perspiration and Basal Metabolism in Three Hundred Combined Observations from Infancy Through Old Age*

| Insensible Perspiration, Gm. per Hour | Metabolism, Calories per 24 Hours | | | | | | | | | | | | f-Insensible Perspiration, in Class Units | y | fy | fy² | fXy |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 0-199 | 200-399 | 400-599 | 600-799 | 800-999 | 1,000-1,199 | 1,200-1,399 | 1,400-1,599 | 1,600-1,799 | 1,800-1,999 | 2,000-2,199 | 2,200-2,399 | | | | | |
| 0- 4 | 4 | 1 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | 5 | —5 | —25 | 125 | 120 |
| 5- 8 | .. | 26 | 1 | .. | .. | .. | .. | .. | .. | .. | .. | .. | 27 | —4 | —108 | 432 | 428 |
| 9-12 | .. | 12 | 17 | 1 | .. | .. | .. | .. | .. | .. | .. | .. | 30 | —3 | —90 | 270 | 303 |
| 13-16 | .. | .. | 2 | 17 | 11 | .. | .. | .. | .. | .. | .. | .. | 30 | —2 | —60 | 120 | 102 |
| 17-20 | .. | .. | .. | 22 | 27 | 7 | 1 | .. | .. | .. | .. | .. | 57 | —1 | —57 | 57 | 70 |
| 21-24 | .. | .. | .. | .. | 31 | 14 | 8 | 1 | .. | .. | .. | .. | 54 | 0 | 0 | 0 | 0 |
| 25-28 | .. | .. | .. | .. | .. | 17 | 8 | 8 | 1 | 1 | .. | .. | 35 | 1 | 35 | 35 | 31 |
| 29-32 | .. | .. | .. | .. | .. | 5 | 7 | 8 | 9 | .. | .. | .. | 29 | 2 | 58 | 116 | 100 |
| 33-36 | .. | .. | .. | .. | .. | .. | 1 | 3 | 8 | 4 | 1 | .. | 17 | 3 | 51 | 153 | 156 |
| 37-40 | .. | .. | .. | .. | .. | .. | .. | 1 | 2 | 6 | .. | .. | 9 | 4 | 36 | 144 | 128 |
| 41-44 | .. | .. | .. | .. | .. | .. | .. | .. | .. | 3 | .. | 1 | 4 | 5 | 20 | 100 | 90 |
| 45-48 | .. | .. | .. | .. | .. | .. | .. | .. | .. | 3 | .. | .. | 3 | 6 | 18 | 108 | 72 |
| F | 4 | 39 | 20 | 40 | 69 | 43 | 25 | 21 | 20 | 17 | 1 | 1 | 300 | | —122 | 1,660 | 1,600 |
| X | —5 | —4 | —3 | —2 | —1 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | | | | | |
| FX | —20 | —156 | —60 | —80 | —69 | 0 | 25 | 42 | 60 | 68 | 5 | 6 | = —179 | | | | |
| FX² | 100 | 624 | 180 | 160 | 69 | 0 | 25 | 84 | 180 | 272 | 25 | 36 | = 1,755 | | | | |
| FXy | 100 | 580 | 177 | 118 | 49 | 0 | 24 | 74 | 153 | 280 | 15 | 30 | = 1,600 | | | | |

The arbitrary origin of X = 1,100 calories; of y = 22 Gm. of insensible perspiration

The first moments about these origins are:
c = —0.597 class units × 200 calories = —119 means of X = 981 calories
d = —0.407 class units × 4 Gm. = —1.63 Gm. means of y = 20.37 Gm. per hour

The second moments about these origins are:
$\sigma X^2 = 5.85 - (-0.597)^2 = 5.48$
$\sigma y^2 = 5.53 - (-0.407)^2 = 5.364$

$\sigma X = 2.342 \times 200 = 468$ calories
$\sigma y = 2.316 \times 4 = 9.26$ Gm.

The cross product about the means = P = 5.33 — (—0.407) (—0.597) = 5.09

$$\text{The correlation coefficient} = \surd = \frac{P}{\sigma X \sigma y} = \frac{5.09}{2.342 \times 2.316} = 0.939$$

$$\text{Probable error} = \frac{0.6745\,(1 - \surd 2)}{\sqrt{300}} = 0.0045$$

To verify the reliability of such a prediction, the curve shown in chart 1 was reproduced in chart 2, and about it were plotted control observations, which included our fifty-six additional observations on older children and twelve observations previously made by Levine on eight infants (shown as circles [13]). It may be seen that all the values for observations on infants deviate more than 15 per cent from our projected curve. This will be discussed later. Of the fifty-six observations on older children, we noted that with the exception of twelve individual scatter points all fell within 15 per cent of the smoothed curve. Omitting for the moment these twelve points, the deviation of the predicted values from those actually determined for the basal metabolism averages plus 1 per cent for the entire series.

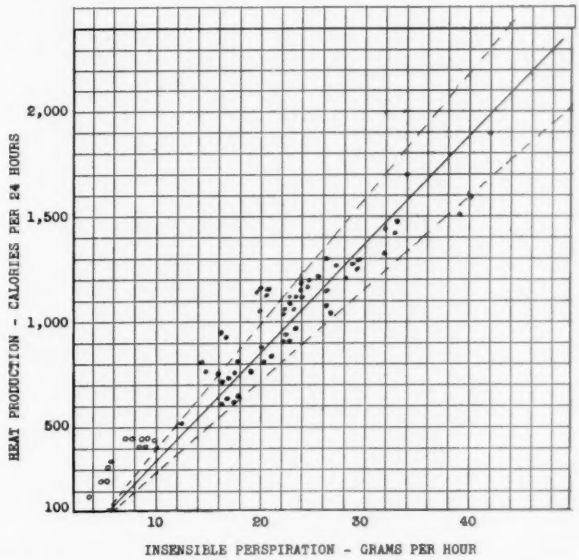


Chart 2.—A proposed curve for predicting the heat production of children (from 4 to 15 years of age) from their insensible perspiration, as measured with the Sauter balance. The dotted lines represent a deviation of 15 per cent from the smoothed curve. The points represent fifty-six control observations of the metabolism and the insensible perspiration of twenty-seven children (hospital normal and abnormal). The circles represent twelve observations previously made by Levine on eight infants.

In twenty-one of the fifty-six observations the basal metabolism was found to be abnormally high and in six abnormally low. In the twenty-seven children with an abnormal basal metabolism, a high degree of correlation was noted between the metabolism and the insensible loss

13. Exact figures for these twelve observations were not available; the circles were approximated from chart 6 in the article by Levine and Marples.[6d]

of weight. The existence of a close correlation even in the presence of an abnormal energy exchange has been pointed out by Soderstrom and DuBois,[7] Levine and Wilson,[6a] Jores,[3] Magendantz,[5] Heller and Schwarz [4] and Benedict and his co-workers.[1]

The twelve observations on older children which gave values that fall outside the 15 per cent deviation zone were made in cases in which there was either evident or possible alteration in the water metabolism. In cases 4 and 20 there was frank clinical evidence of an alteration in tissue hydration. In case 14 a diagnosis of diabetes insipidus was considered, though not entirely substantiated. The patients in cases 6 and 9 were diabetic children for whom control observations showed an accepted correlation between the metabolism and the insensible perspiration. With the omission of a dose of insulin, however, the measured metabolism in these cases exceeded the predicted value by more than 15 per cent. This fact is of considerable interest and should be considered when one is making a large series of observations. The discrepancy in correlation when the patient is deprived of insulin may be intimately connected with an alteration in the water exchange. The patient in case 17 was a child with myeloid leukemia who had a basal metabolism of plus 23 per cent and an insensible loss of weight of 39.41 Gm. per hour. He was treated with high voltage roentgen therapy and in the course of a few weeks showed definite clinical improvement. A previously enlarged spleen shrank until it was no longer palpable, and the basal metabolism dropped to minus 5 per cent after ten treatments. Frequent determinations of the metabolism and the insensible loss of weight were made during the course of treatment. These showed a gradual approximation of the measured to the predicted values. The cause of this improvement in correlation under the influence of high voltage roentgen therapy is difficult to explain. Whether the underlying factor is an abnormal water exchange in leukemia and whether high voltage roentgen therapy influences elimination of water may well be the subjects of further study.

The striking divergence from the prediction curve in cases in which the water metabolism was disturbed has been reported by previous investigators,[14] who stressed excessive tissue hydration as a source of error in predicting the total energy metabolism from the insensible perspiration.

From the combined series of three hundred observations on infants, adults and older children, a statistically derived curve is plotted in chart 3. This curve shows little difference in slope from that of the

14. Manchester, R. C.; Husted, C., and McQuarrie, I.: J. Nutrition **4**:39, 1931. Robert, F.: Arch. f. exper. Path. u. Pharmakol. **164**:367, 1932. Lavietes, P. H.: J. Clin. Investigation **14**:57, 1935.

curve in chart 2, derived from our one hundred observations on children only. Our fifty-six control observations and the twelve observations on infants assume a scatter almost identical with that in chart 2. The same twelve scatter points referring to older children and all those referring to Levine's infants deviate more than 15 per cent from the smoothed curve. This is what might be expected from the striking similarity of the two curves.

It is apparent from the uniform deviation of the observations on infants that our prediction curve proposed for older children does not hold for the younger ones. In attempting to combine our proposed curve for predicting the heat production of older children with that proposed

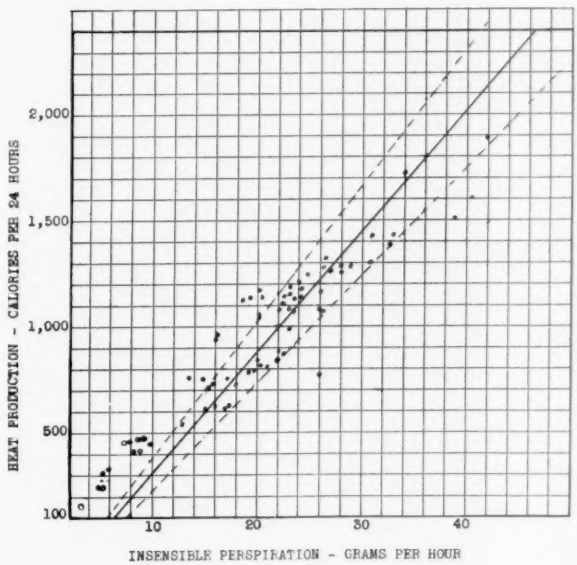


Chart 3.—A statistically derived curve showing the trend of the basal metabolism and the insensible perspiration in three hundred observations on infants, adults and children. The broken lines represent a ±15 per cent deviation from the smoothed curve. The points and the circles refer to the same control observations as those indicated in chart 2.

by Levine for infants [15] we found a change in the slope of the curves at their junction. This change expresses itself as a flattening. Levine observed such a flattening of the curves of basal metabolism and insensible perspiration in the region of from 500 to 600 calories and from 10 to 12 Gm. This region coincides with the age period immediately following the first year of life. Benedict previously pointed out that

15. This curve is shown in chart 6 in Levine and Marples.[6d]

the curves of growth, of increase in height and weight and of total heat production are less steep after the first year of life.[16] It is therefore not surprising that curves representing functions of these variables also flatten out at a corresponding period.

Attempts to explain the difference between the slope of the curve for the first year of life and that for the succeeding age period have implicated differences in water metabolism. It seems to us that the lack of strictly comparable conditions requisite for metabolic studies of infants may be of some importance in this connection. It should be remembered that studies of basal metabolism are necessarily made on infants after they have been fed and are asleep, while older children and adults are studied in the postabsorptive state and while awake.

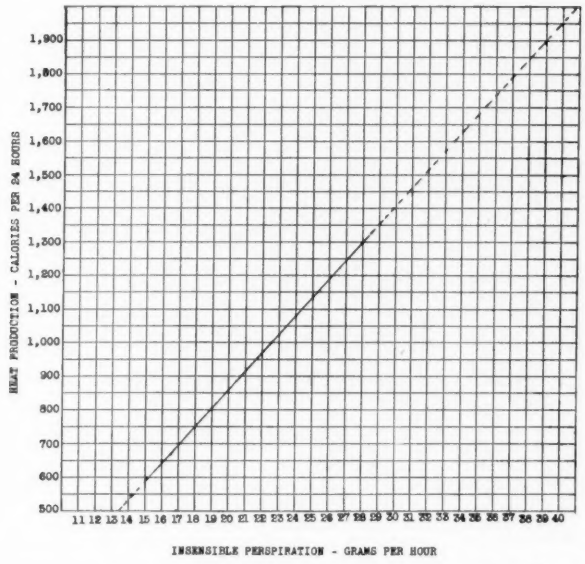


Chart 4.—The same curve as that in chart 2, reproduced without the scatter points for clarity. The broken portions of the curve represent periods for which further corroborative data are necessary.

Levine's proposed curve for predicting the basal metabolism of infants from their insensible loss of weight begins at 100 calories and extends to about 600. He pointed out that the last portion of his curve requires additional confirmation. Our observations for this period are too few to be significant.

Our proposed curve for older children begins at 600 calories and extends to 1,300. Below 600 and above 1,300 the curve is projected

16. Benedict, F. G., and Talbot, F. B.: Metabolism and Growth from Birth to Puberty, Publication 302, Carnegie Institution of Washington, 1921.

to include a few isolated observations. Further corroborative data are needed for these portions of the curve. For purposes of clarity, the curve is reproduced in chart 4 without the scatter points.

## SUMMARY AND CONCLUSIONS

Additional experimental data are presented that substantiate the correlation between the basal metabolism and the insensible perspiration in the age group of from 4 to 15 years. These data were obtained through independent measurements of the basal metabolism (Benedict-Roth apparatus) and the insensible loss of weight (Sauter balance) in one hundred observations made on forty-four hospital normal children.

A statistical analysis of the data thus collected shows a high degree of positive correlation (table 2).

A statistically derived curve based on these data is proposed for the prediction of the basal metabolism from the insensible perspiration for the age group studied (chart 4).

This curve, experimentally controlled by fifty-six further observations, made on twenty-seven additional children, shows a high degree of reliability for children with normal or abnormal energy exchange, except under certain conditions of evident or presumed derangement of water metabolism.

The slope of our proposed prediction curve for children is less steep than the slope of Levine's curve, previously proposed, for infants. Flattening occurs in a zone which corresponds to about the end of the first year of life.

# THE VARIABLE COURSE OF PERTUSSIS

## DOES HAEMOPHILUS PERTUSSIS UNDENATURED BACTERIAL ANTIGEN ALTER IT?

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The appearance of reports, in general favorable, on the therapeutic value of Haemophilus pertussis undenatured bacterial antigen (Krueger [1]) stimulated in us a desire to observe carefully a small number of treated patients, together with suitable control children. The duration of pertussis may vary naturally tenfold. We have seen cases in which the duration was eight days (verified by positive cough plates) and cases in which it was more than eighty days. The frequency of the paroxysms is dependent on innumerable variables, many of which are not understood. It is of course reasonable to suppose that different persons vary tremendously in specific resistance (immunity) and in nonspecific resistance. Frawley [2] expressed the belief that the allergic child is more likely to have severe attacks. In regard to age, adults in general have mild attacks, often no doubt because of a clinical or subclinical previous attack which has left a partial immunity. However, severe and mild attacks are seen at all ages. We have seen an attack of three weeks' duration, without whooping or vomiting, in a 2 year old infant. Luttinger [3] and Herman and Bell [4] have recorded a higher mortality for girls than for boys, and it may be inferred that girls are likely to have the disease more severely. The environment of the patient has of course a great bearing on the severity of the attack. Temperature, humidity, wind, dust, noise and general comfort, in other words, living conditions, influence the duration and severity of the disease.

It was felt that in the published reports, which will be summarized, this great variability in the severity and the duration of pertussis is not fully considered. The difficulty of evaluating any therapeutic agent for

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From the Department of Pediatrics and the George Williams Hooper Foundation for Medical Research, University of California Medical School.

1. Krueger, A. P.; Nichols, V. C., and Frawley, J. M.: Proc. Soc. Exper. Biol. & Med. **30**:1097, 1933.

2. Frawley, J. M.: J. Pediat. **7**:692, 1935.

3. Luttinger, P.: The Epidemiology of Pertussis, Am. J. Dis. Child. **12**:290 (Sept.) 1916.

4. Herman, C., and Bell, T.: Tr. Am. Pediat. Soc. **35**:132, 1923.

this disease is notorious. With regard to treatment with vaccine or specific antigen (such as injections of H. pertussis undenatured bacterial antigen), it must be recalled that Bayer [5] found the psychotherapeutic effect of injections of distilled water helpful. We have therefore attempted to scrutinize the effect of injections of H. pertussis undenatured bacterial antigen and of a control solution on the course, or, more logically, the courses, of the disease.

Frawley, Stallings and Nichols [6] reported favorably on the therapeutic effect of H. pertussis undenatured bacterial antigen on a series of 165 children. A control group is not described. Injections were given daily or every other day, beginning with a dose of 0.1 cc. intradermally and 0.1 cc. subcutaneously. The subcutaneous dose was increased until a total of 1 cc. was given. The authors' summary is quoted: "Eighty-six of these (165) had been coughing less than one week. Sixty-nine per cent of this group gave good response to treatment, with cessation of severe symptoms in less than a week. Seventy-nine were seen later than one week after the onset of the coughing. Treatment in these was not particularly successful, only 45 per cent showing a cessation of severe symptoms within a week."

Munns and Aldrich,[7] using a total of 2.5 cc. of this agent given on alternate days in doses of 0.5, 1 and 1 cc. each, treated 74 children in whom the disease was clinically established. Of these, 48 had mild attacks. The authors noted that "in 36 instances mothers reported definite abatement of cough within twelve to twenty-four hours following injections of the antigen." They concluded that the undenatured bacterial antigen is of most value if given within the first seven days of the disease (or before the onset). They suggested the use of larger and more numerous doses. No control group was observed at the time of their study.

Stallings and Nichols,[8] in a series of 232 cases, used an initial dose of 0.1 cc. and increased this gradually to 1 cc. The injections were given daily or every other day. When the latter method was used "in severe cases it was noticeable that the coughing was much more severe on the day when no injections were given." The number of injections varied from four to eighteen. They were given until "symptoms abated." Subsidence of severe symptoms within a week after institution of treatment occurred in 77.6 per cent of the patients. When treatment was started in the paroxysmal stage results were as good as

5. Bayer, W.: Med. Klin. **28**:1459, 1932.

6. Frawley, J. M.; Stallings, M., and Nichols, V. C.: J. Pediat. **4**:179, 1934.

7. Munns, G. F., and Aldrich, C. A.: J. Pediat. **5**:590, 1934.

8. Stallings, M., and Nichols, V. C.: Treatment of Whooping Cough with an Active Undenatured Antigen, Am. J. Dis. Child. **48**:1183 (Dec.) 1934.

when it was begun in the catarrhal stage. The average total duration of the disease in the 232 treated patients was four weeks, as compared to seven weeks in a control group of 165 patients. The duration of severe symptoms in the test group averaged ten days and in the control group three weeks. These authors are quoted: "The mechanism of action in the infected person has not been experimentally determined, but observations on intelligent adults with severe pertussis show in from two to three hours an alleviation of symptoms lasting twenty to twenty-four hours. Symptoms recur after this time and are relieved by the next injection. In this respect the mechanism appears to be a desensitization."

After the present study had been in progress some time, a second report by Frawley [2] on the therapeutic use of H. pertussis undenatured bacterial antigen appeared. This author had increased his daily dose tenfold. He treated 26 children with injections of 5 cc. twice a day for a period of from five to seventeen days. When he instituted treatment during the first week, in 10 of 12 cases the disease was mild. When injections were begun after the tenth day, in 11 of 14 cases the condition was severe. This finding is at variance with that of Stallings and Nichols, who, as has been mentioned, obtained equally satisfactory results regardless of whether treatment was initiated in the catarrhal or in the paroxysmal stage.

In the present study we particularly desired to examine the rapid abatement of paroxysms described by Stallings and Nichols as occurring within a few hours after injections. If we could confirm this finding it would then be necessary to show whether its mechanism was a specific desensitization or a reaction either of fear or of suggestion on the part of an impressionable child. If this rapid diminution in the frequency of paroxysms occurred in an infant under 1 year old, it might reasonably be supposed to be a specific one.

The method used for observing patients was that described by Kerley [9] thirty years ago. He recorded the number of paroxysms of coughing occurring in twenty-four hour periods. After the peak of frequency had been reached, trial of various drugs was instituted. Antipyrine and bromide were found most effective in reducing the number of paroxysms. In 1925, Faber and Struble [10] utilized the same method in studying the effect of roentgen treatment on pertussis. The parents of their patients were instructed to record by twenty-four hour periods the number of paroxysms (defined as an attack of coughing

9. Kerley, C. G.: Treatment of Diseases of Children, Philadelphia, W. B. Saunders Company, 1907, p. 321.

10. Faber, H. K., and Struble, H. P.: Does Roentgen Ray Modify the Course of Whooping Cough? J. A. M. A. **85**:815 (Sept. 12) 1925.

followed by a definite whoop). A control group, children treated with antipyrine and bromide, were similarly observed during the same epidemic. From the data obtained, a curve of the average frequency of paroxysms during the course of the paroxysmal stage of the disease was constructed for each group. The two curves were almost identical. The frequency of paroxysms rose rapidly, attaining a peak of about fourteen between the fifth and the tenth day. It then fell rapidly, reaching eight or nine by the fifteenth day. Thereafter the decline was gradual, the base-line being reached between the ninth and the tenth week. Similarly, a curve of the average number of attacks of vomiting for each of the two groups was obtained. By this method Faber and Struble found that the frequency of paroxysms for the two groups was similar and clearly demonstrated that roentgen treatment has no advantage over antipyrine and bromide in diminishing the frequency of attacks.

Bamberger and Menke [11] recently made a careful statistical study of the course of untreated pertussis. Their report appeared after the commencement of our study. They recorded the number of whoops ("reprises") given in twenty-four hour periods by 100 hospitalized patients. The disease was described as "in general severe, for the patients were hospitalized." From these data they constructed curves of the mean daily number of whoops and their probable errors during the course of the disease. They found that the peak of frequency was reached between the eighth and the twelfth day of whooping. They concluded that these curves might serve as a base-line for future studies on the efficacy of therapeutic agents in pertussis. They made the point that if the agent is used before the peak of frequency is reached it is impossible to judge its effect because the disease might have been mild anyway. This statement is certainly rational. It opens to critical scrutiny the advocacy of an agent "which is effective if given early in the course of the disease." Bamberger and Menke advanced evidence indicating that once the peak of frequency (an average of from ten to fifteen whoops a day) is reached the frequency of whooping declines at a certain demonstrated gradient. They maintained that alteration of the slope of this gradient is the only criterion by which the effectiveness of a therapeutic agent may be judged.

It is of interest that the shape and the height of the curves obtained by Faber and Struble and by Bamberger and Menke are similar.

Bamberger and Menke also demonstrated that marked daily variations in the number of whoops are the rule. Thus, between the sixth and the eighth day of the disease 63 per cent of their patients had daily variations of at least four whoops and 11 per cent had daily variations

11. Bamberger, P., and Menke, H.: Klin. Wchnschr. **14**:1036, 1935.

of more than nine whoops. They charted the probable variation in the number of whoops occurring from day to day at different periods of the disease and showed that there is a slight tendency for the daily variation to decrease as the disease progresses. It is this normal daily variation in the frequency of attacks that further increases the difficulty of evaluating any therapeutic agency.

The defining of a paroxysm, as done by Faber and Struble, as "a coughing spell followed by a definite whoop" and the charting of whoops ("reprises") only, as done by Bamberger and Menke, have the advantage of clarity, particularly for parents. The definition used by Faber and Struble, however, is not entirely correct, since severe attacks of coughing, with or without deep inspirations and often with cyanosis and vomiting, are frequently seen without any whoops being heard. This is common knowledge. Kerley mentioned that "often the very young and the very delicate do not whoop even during a severe attack." Knoepfelmacher,[12] Benson [13] and others have made the same remark. We have observed severe seizures in adults also without any audible whoop. It is therefore felt that the definition used by Faber and Struble is hardly adequate and that in charting only the whoops Bamberger and Menke tended to decrease the actual number of paroxysms that may have occurred. In this paper the word paroxysms is defined as a sudden attack of violent coughing lasting more than thirty seconds. It was so defined to the parents. Mild paroxysms are usually not followed by a whoop. In contrast with the mild type, severe paroxysms, except in infants and adults, are usually followed by a whoop. The relation of vomiting to whooping is inconstant. One or the other or both may be present. A 5 year old girl is recalled who vomited after most of her paroxysms but was never heard to whoop.

In this paper are summarized for 45 cases the total duration of coughing, the duration of the stage of catarrhal cough, the duration of the stage of paroxysms, the maximum number of paroxysms in one twenty-four hour period, the day of the paroxysmal stage when this maximum was obtained, the number of days the patient vomited, the maximum number of vomitings in one twenty-four hour period and the presence or absence of facial edema and of hemorrhage. In 1 case only the injections of H. pertussis undenatured bacterial antigen were begun before (one day before) the onset of coughing. In 10 cases injections were begun in the catarrhal period, and in 17 cases injections were begun after the onset of paroxysms. Seventeen control children

12. Knoepfelmacher, W., in von Pfaundler, M., and Schlossmann, A.: The Diseases of Children, translated by M. G. Peterman, Philadelphia, J. B. Lippincott Company, 1935, vol. 3, p. 326.

13. Benson, W. T.: Brit. M. J. **1**:657, 1935.

were observed, 6 of whom received injections of a control material. This control material was a 1 to 300 dilution of H. pertussis undenatured bacterial antigen in physiologic solution of sodium chloride. Certainly the solution of sodium chloride itself would have been preferable, but policy necessitated the inclusion of 0.1 cc. of the antigen in every 30 cc. of the solution used. We do not believe that the resulting amount of protein in the control solution used (0.00003 mg. per cubic centimeter) could alter its value as a control.

The H. pertussis undenatured bacterial antigen used in this study came from two different lots.[14] The first contained 1 mg. of protein nitrogen per hundred cubic centimeters and 10 mg. of total nitrogen per hundred cubic centimeters. The second lot contained 2.25 mg. of protein nitrogen per hundred cubic centimeters and 10 mg. of total nitrogen per hundred cubic centimeters. In three instances in which the injections did not appear to be helping the child, other lots of unknown protein content were purchased and used. The total amount given to a single child varied from 2.5 cc. to 75 cc. The total amount of protein nitrogen varied from 0.025 to 1.125 mg. Injections were usually given daily but in some instances were given every two or three days. Early in the trial 1 cc. was used as the initial dose. Later this was increased to 5 cc. and in two instances to 10 cc., 5 cc. bilaterally. On only two occasions was the local reaction marked enough to cause complaint from the parent. These reactions were to a single injection of 7 cc. (0.07 mg. of protein nitrogen). The agent was injected both subcutaneously and intradermally—from 0.1 cc. to 0.2 cc. being given intradermally and the remainder subcutaneously.

The group studied (table) consisted of infants and children from 7 weeks to 7 years of age. The age distribution in the test and that in the control group were similar. There were 15 boys and 13 girls in the test group. There were 13 boys and 4 girls in the control group. The preponderance of boys may have given an advantage to the control group because, as was mentioned previously, Luttinger [3] and Herman and Bell [4] found the mortality higher for girls. However, in our small series of cases the severity of the disease as indicated by the criteria used was not greater in the girls. No deaths occurred. The only complication was otitis media in 2 patients, a girl in the test group and a boy in the control group.

In addition to giving injections, it was usually necessary to put the children to bed, to use an abdominal binder and to resort to sedatives. (Benson has advised confinement to bed when the paroxysms exceed thirty in twenty-four hours.) Seven of the 28 test patients and

14. The antigen used in this study was supplied by Eli Lilly & Co. and was the product designated by them "H. pertussis undenatured bacterial antigen."

2 of the 17 control patients received no drug therapy. Phenobarbital was used, often being alternated with a mixture of antipyrine and bromide. One is forced to admit that the use of this additional medication in such a study is undesirable from a scientific point of view. It is also evidence of the inadequacy of the specific parenterally administered therapy.

Positive cough plates were obtained in all but 6 cases. In these the diagnosis was obvious.

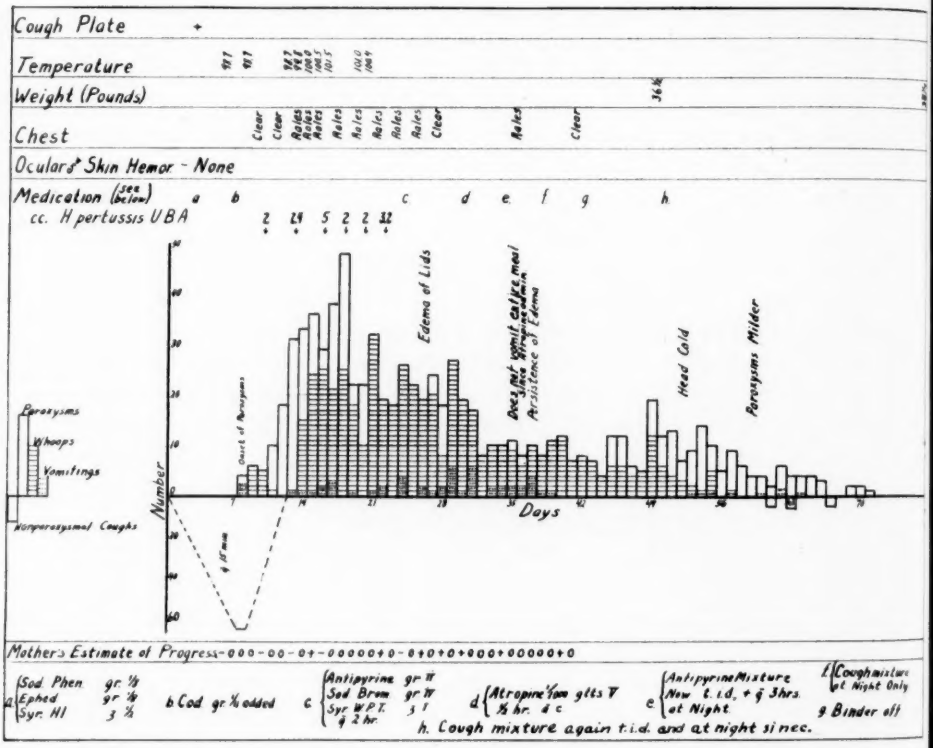
Cough Plate
Temperature
Weight (Pounds)
Chest
Ocular & Skin Hemor. - None
Medication (see below)
cc. H pertussis U B A
Paroxysms
Whoops
Vomitings
Nonparoxysmal Coughs
Number
Days
Edema of Lids
Does not vomit after meal
Head Cold
Paroxysms Milder
Mother's Estimate of Progress
a (Sod. Phen. gr ½ Ephed. gr ¼ Syr. Hi ½)
b Cod. gr ½ added
c (Antipyrine gr IV Sod. Brom. gr IV Syr. W.P.T. ½ I q 2 hr.)
d (Atropine ¹/₂₀₀ gtts V ½ hr. a c)
e (Antipyrine Mixture Now t.i.d. + q 3 hrs. at Night)
f (Cough mixture at Night Only)
g Binder off
h. Cough mixture again t.i.d. and at night si nec.

Chart 1.—Summary of data on G. P., a girl 4 years old. In charts 1, 2, 5 and 6 the following abbreviations for drugs are used: Sod. Phen. for sodium phenobarbital; Ephed. for ephedrine; Syr. Hi. for syrup of hydriodic acid; Cod. for codeine; Sod. Brom. for sodium bromide, and Syr. W. P. T. for syrup of white pine tar.

## RESULTS

In charts 1 to 7 are illustrated the course of the disease in 7 cases.

Charts 1 and 2 are the records of a sister and brother. The former (G. P.) began to receive injections before the peak of frequency of the paroxysms was reached. The doses used were slightly larger than those recommended by Munns and Aldrich and Stallings and Nichols, but much smaller than the 5 cc. twice a day

recommended by Frawley in his second paper.[2] It is obvious that the early injections in no way hindered the development of a high peak. The child suffered severely. All the drugs usually recommended were called on to aid H. pertussis undenatured bacterial antigen. In explanation of the diagram, the height of each column represents the total number of paroxysms. Paroxysms followed by a whoop are indicated by a bar. Paroxysms followed by vomiting are indicated by small dots. In this case paroxysms without whooping occurred during the second week of the disease and again after the seventh week. Individual nonparoxysmal

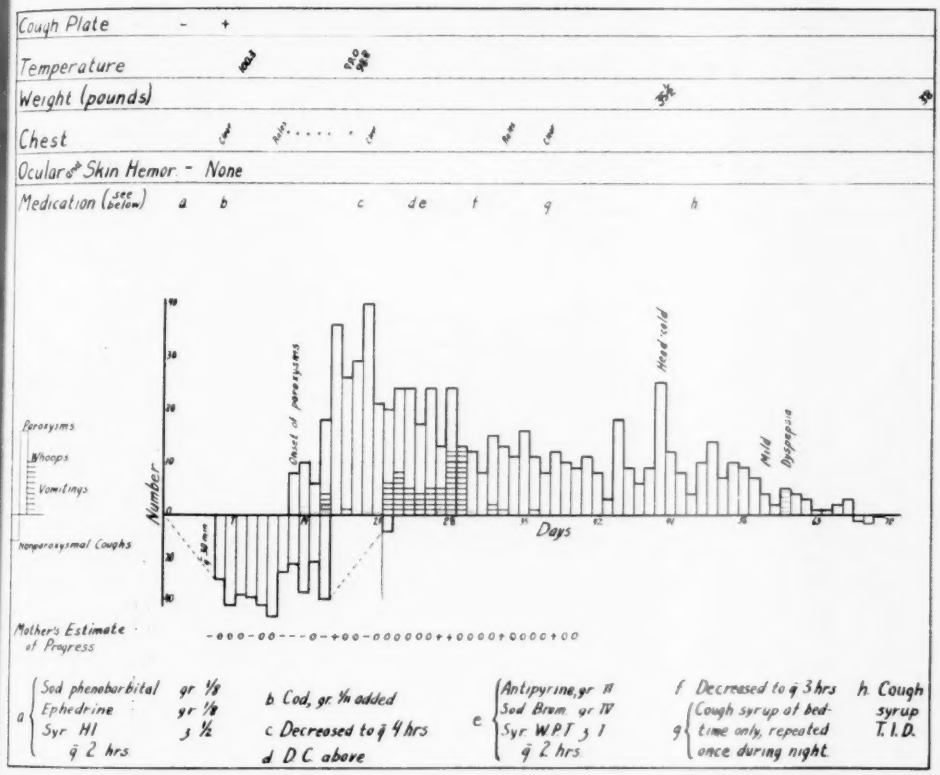
Cough Plate - +
Temperature
Weight (pounds)
Chest
Ocular & Skin Hemor. - None
Medication (see below) a b c d e f g h
Paroxysms
Whoops
Vomitings
Nonparoxysmal Coughs
Mother's Estimate of Progress
Number
Onset of paroxysms
Hard cold
Mild bronchitis
Days
a Sod phenobarbital gr ½ Ephedrine gr ⅛ Syr HI ʒ ½ q 2 hrs
b Cod, gr ⅛ added
c Decreased to q 4 hrs
d D C above
e Antipyrine, gr II Sod Brom gr IV Syr W.P.T ʒ 1 q 2 hrs
f Decreased to q 3 hrs
g Cough syrup at bedtime only, repeated once during night
h Cough syrup T.I.D.

Chart 2.—Summary of data on A. P., a boy 3 years old, the brother of G. P.

coughs were too frequent to be recorded by the highly intelligent parent. They are merely indicated by the triangular dotted line below the abscissa. In this instance the catarrhal period lasted seven days.

The brother (A. P., chart 2) received no injection of any kind. Otherwise the medication was the same. His condition was likewise severe and prolonged. Less cyanosis was evident during paroxysms, however, and, as the chart indicates, inspiratory stridor (whoop) was infrequently heard. The duration of his catarrhal period was fairly long—twelve days. Marked daily variations in the number of paroxysms are evident.

Charts 3 and 4 illustrate the course of the disease in 2 children in another family. In these cases the attacks were even more similar. Their duration was practically the same. The 2½ year old girl (C. N.) received daily injections of

2 cc. of H. pertussis undenatured bacterial antigen for twelve days. These injections may of course have prevented the appearance of a peaklike rise in the frequency of the paroxysms. The 3½ year old boy (Ch. N.) received daily injections of the control solution. The series of plus signs on the diagram opposite "Mother's Estimate of Progress" indicates that for eight consecutive days the boy was each day "better"—although the frequency of his paroxysms did not decrease. The frequency curve for this control patient fails, as does that of his sister, to show the typical peak.

Charts 5 and 6 (E. G. and C. G.) illustrate the cases of two brothers. E. G. was treated with injections of H. pertussis undenatured bacterial antigen. An initial

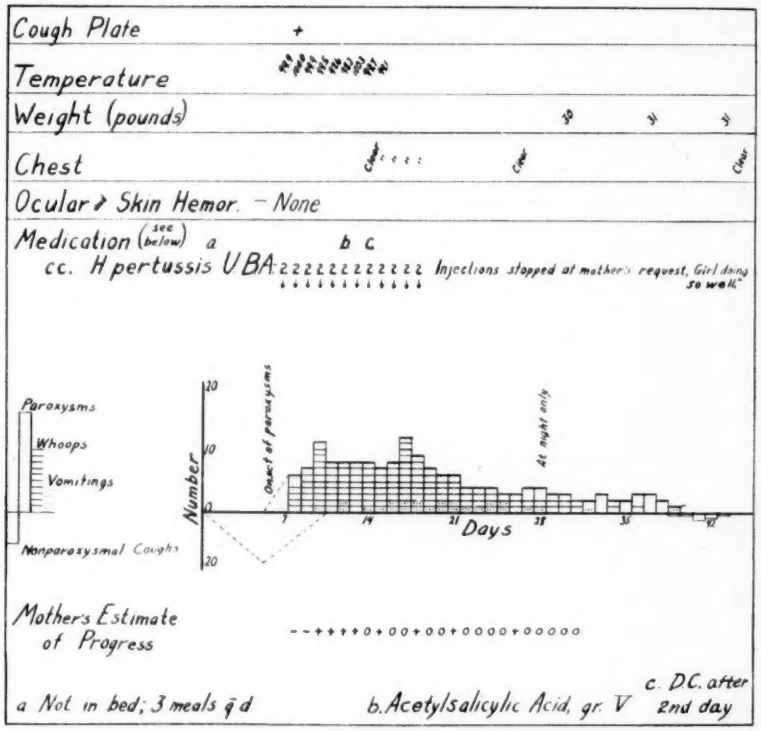


Chart 3.—Summary of data on C. N., a girl 2½ years old.

dose of 3 cc. was used in the evening of the fourth day of the paroxysmal stage, which was the eleventh day of the disease. The marked drop in the number of vomitings charted on the thirteenth day took place in the twenty-four hour period just before the second injection (6:30 p. m.). It cannot be due to the second injection and can be explained only as a chance variation. Further examination of the diagram shows that in the twenty-four hours after the second injection there was an appreciable increase in the frequency of paroxysms and vomiting. Their peak was attained. In other words, the contrary of the rapid abatement of seizures described by Stallings and Nichols was observed. The dose was then increased to 5 cc. The frequency of vomitings rapidly diminished, and after the fifth injection the frequency of paroxysms decreased. It is certainly possible that the four doses

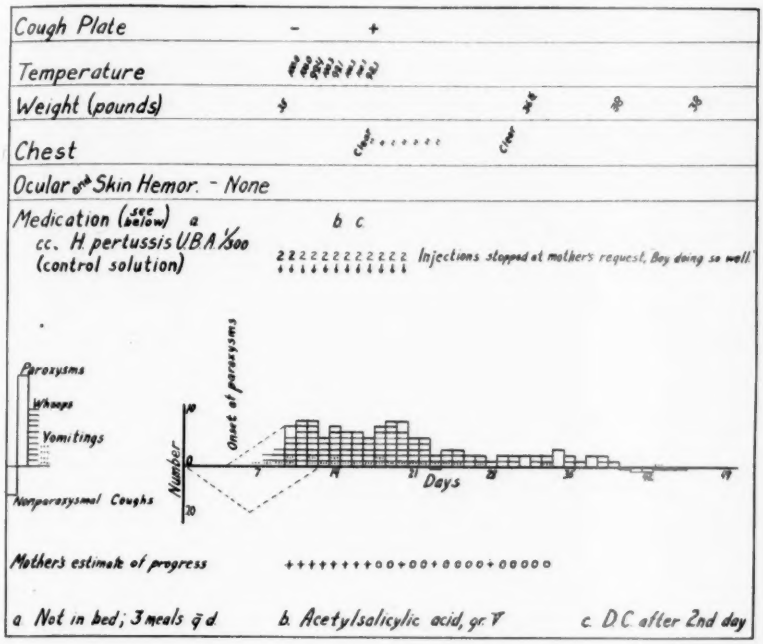


Chart 4.—Summary of data on Ch. N., a boy 3½ years old.

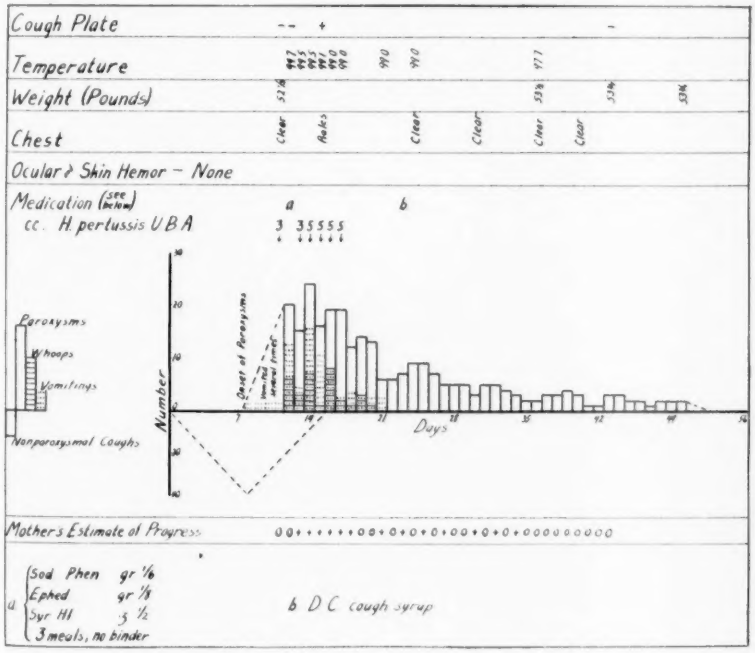


Chart 5.—Summary of data on E. G., a boy 7½ years old.

of 5 cc. affected this drop. On the other hand, the warning of Bamberger and Menke should be considered, i. e., that treatment given at the acme of the disease always gives good results because thereafter the number of seizures normally decreases.

The younger brother (C. G., chart 6) was given injections of the control solution. They were associated with a decrease in the frequency of paroxysms but with an increase in the frequency of vomiting. He was definitely more prostrated than his brother. The psychotherapy did not affect the parent, who told us that the boy's condition remained about the same after he received the injections. This case presents an example, of which we had several, of the failure of the injection

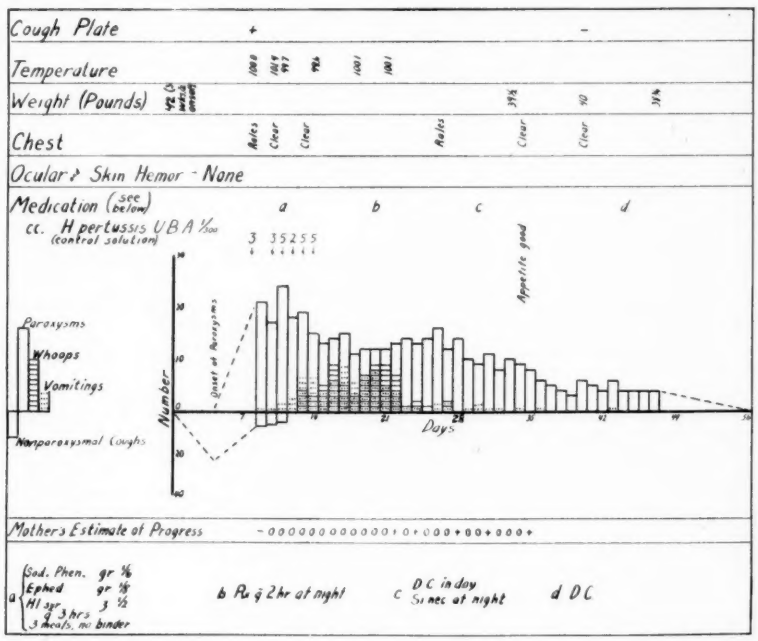


Chart 6.—Summary of data on C. G., a boy 4 years and 10 months old.

per se. We were not so fortunate as Bayer was with this form of treatment. Incidentally, both these brothers whooped hardly at all, although they vomited more than most children.

Chart 7 (R. P.) illustrates a case in which the advice of Bamberger and Menke was followed. Treatment was not begun until after the peak of paroxysms was passed. No drugs were administered to the patient. (The drop from nineteen to ten paroxysms recorded on the day of the first injection indicates that in the twenty-four hours prior to the injection there were only ten paroxysms.) Large doses were then given the little girl, in an attempt to depress sharply the normal declining gradient of seizures. Her progress was satisfactory. The H. pertussis undenatured bacterial antigen may have played a part; it is impossible to say definitely. The condition was never severe; the peak was reached at only nineteen paroxysms.

The small number of the cases studied, the wide variability in the daily frequency of paroxysms and the variability in the dose used and in the time of beginning treatment prevent the construction of average frequency curves of the course of the paroxysms. We have not, therefore, curves for our test and our control group which could be compared to the curves of Faber and Struble and of Bamberger and Menke. However, the scatter diagram (chart 8) serves a similar purpose and is statistically more reliable. Therein is recorded the daily total number

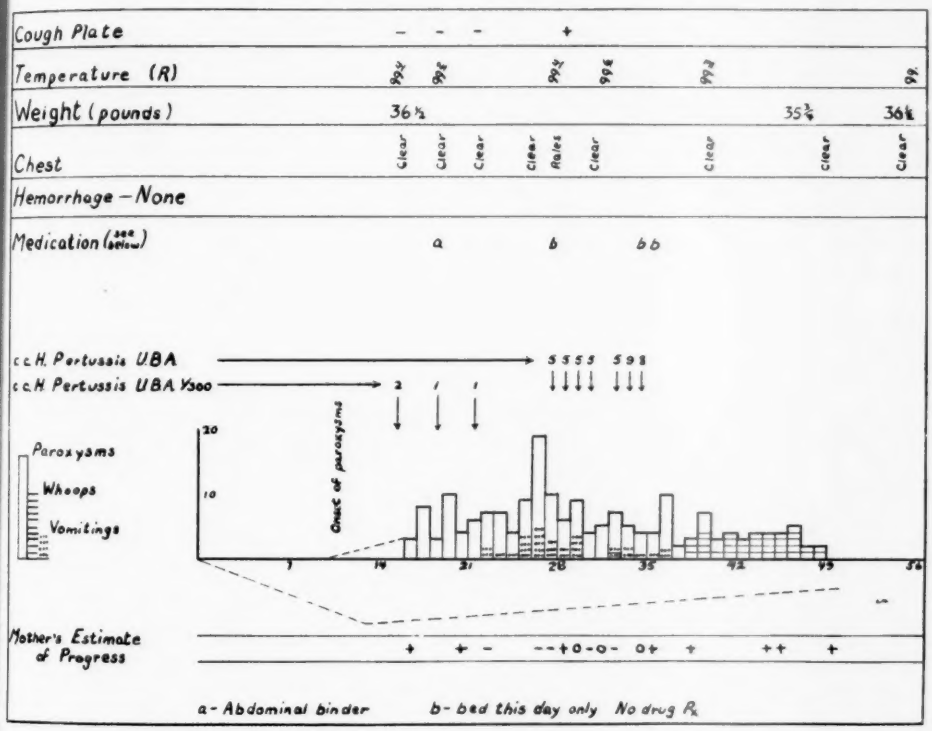


Chart 7.—Summary of data on R. P., a girl 4 years old.

of paroxysms (ordinate) for the duration of the paroxysmal stage (abscissa). Data for both the treated and the control patients appear.

The small circles indicate the daily totals of paroxysms for all control patients and for treated patients before the beginning of treatment. They represent the frequency of paroxysms in an untreated child. Crosses indicate daily totals of paroxysms for treated patients. Therefore, the totals for a child who received injections in the catarrhal period are recorded as crosses from the beginning in this diagram, whereas the totals for a child who received his first treatment during the

paroxysmal stage are recorded as crosses beginning with the day after the first injection. Before this injection, the frequency of his paroxysms are recorded as circles.

If treatment with H. pertussis undenatured bacterial antigen were effective in reducing the number of paroxysms, there would be a tendency for the crosses to fall while the circles remained usually at a higher level. If the treatment tended to shorten the paroxysmal stage, the

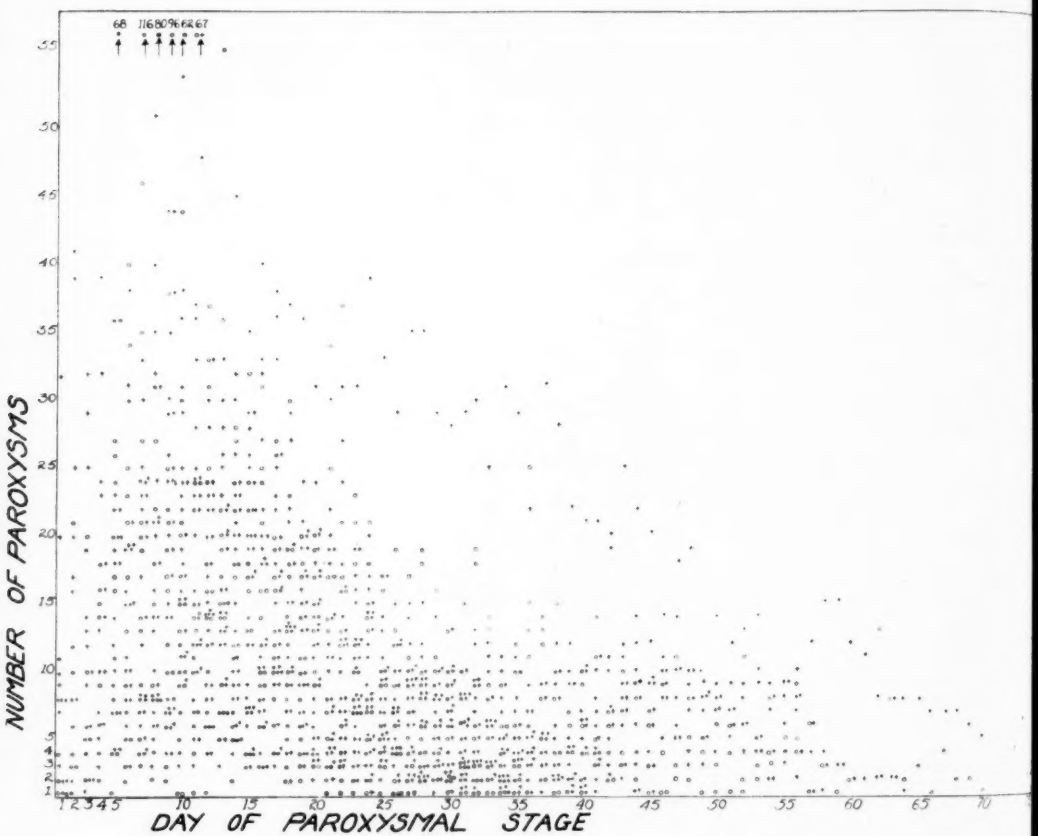


Chart 8.—Scatter diagram showing the daily total of paroxysms during the paroxysmal stage for both the treated and the control patients. O indicates the number of paroxysms in untreated patients, and + indicates the number of paroxysms in patients treated with H. pertussis undenatured bacterial antigen.

circles would persist further to the right along the abscissa than would the crosses. This does not appear to be the case. No tendency for treated patients to have fewer paroxysms or shorter paroxysmal stages is demonstrable. The general picture of the scatter diagram is similar to

the average curves plotted by Faber and Struble and by Bamberger and Menke. A natural tendency for the frequency of seizures to decline is evident about the fifteenth day.

In the table are summarized data on the 28 test and 17 control patients. A decrease in the frequency of paroxysms after injections occurred in only 7 of the 27 treated patients, and decreased severity

*Summary of Data on Forty-Five Children with Pertussis*

| | Children Treated with H. Pertussis Undenatured Bacterial Antigen | | | Control Children | | |
|---|---|---|---|---|---|---|
| | Totals | Range | Mean | Totals | Range | Mean |
| Total number of children | 28 | | | 17 | | |
| Boys | 15 | | | 13 | | |
| Girls | 13 | | | 4 | | |
| Age at onset of disease | | 5 wk. to 7 ½yr. | 3.7 yr. | | 3 mo. to 8 yr. | 5.0 yr. |
| Injections begun | | | | | | |
| One day before onset | 1 | | | 1 } | | |
| In catarrhal stage | 11 | | | 1 } | of control solution | |
| In paroxysmal stage | 17 | | | 4 } | | |
| Total days of injections | | 1 to 14 | 5.5 | | 3 to 12 | |
| Total cc. of antigen given | | 2.5 to 75 | 21.0 | | | |
| Total mg. of protein given | | 0.025 to 1.125 | 0.29 | | | |
| Decrease in frequency of paroxysms during injections | 7 | | | 2 | | |
| Decrease in frequency of vomiting | 3 | | | 0 | | |
| Decrease in severity of paroxysms reported by patient | 9 | | | 4 | | |
| Duration of disease, days | | 39 to 86+ | 57+ | | 20 to 85 | 55+ |
| Duration of catarrhal stage, days | | 2 to 23 | 8.3 | | 2 to 21 | 7.4 |
| Duration of paroxysmal stage, days | | 24 to 78+ | 42.5 | | 7 to 78 | 39.8+ |
| Maximum number of paroxysms in 24 hours | | 4 to 67 | 30.0 | | 5 to 116 | 25.5 |
| Day of paroxysmal stage when maximum occurred | | 1st to 16th | 10th | | 2d to 30th | 12th |
| Total days of vomiting | (3 did not vomit) | 0 to 48 | 14.4 | (2 did not vomit) | 0 to 50 | 14.2 |
| Maximum number of vomitings in 24 hours | | 0 to 16 | 4.7 | | 0 to 16 | 5.4 |
| Edema of eyelids | 22 | | | 11 | | |
| Hemorrhages | 2 | | | 2 | | |
| Rough clinical appraisal | | | | | | |
| Mild | 2 | | | 4 | | |
| Moderate | 20 | | | 9 | | |
| Severe | 6 | | | 4 | | |
| Additional therapy | | | | | | |
| Rest in bed | 19 | | | 11 | | |
| Abdominal binder | 25 | | | 12 | | |
| Medication | 20 | | | 15 | | |
| Appearance of head cold during paroxysmal stage | 12 | | | 7 | | |
| Otitis media | 1 | | | 1 | | |

was reported by the parents for 9. Four of these 9 were among the 7 with decreased frequency. Only 2 of 10 children who received injections of the control solution (including some of the test children who received control injections before the administration of H. pertussis undenatured bacterial antigen was started) showed decreased frequency of paroxysms, whereas mothers reported decreased severity in 5 cases. A parent's report of decreased severity is no doubt the sum of the

specific effect on the child, the psychic effect on the child and the psychic effect on the parent. The relative weight of these components is indeterminable. It is evident, however, that our control injections did not yield as satisfactory results as did Bayer's, even though the children who received the injections were of an impressionable age.

The duration of the disease in the test and the control group showed the same wide variability—from less than one month to almost three months. The mean duration for the two groups was of the same order.

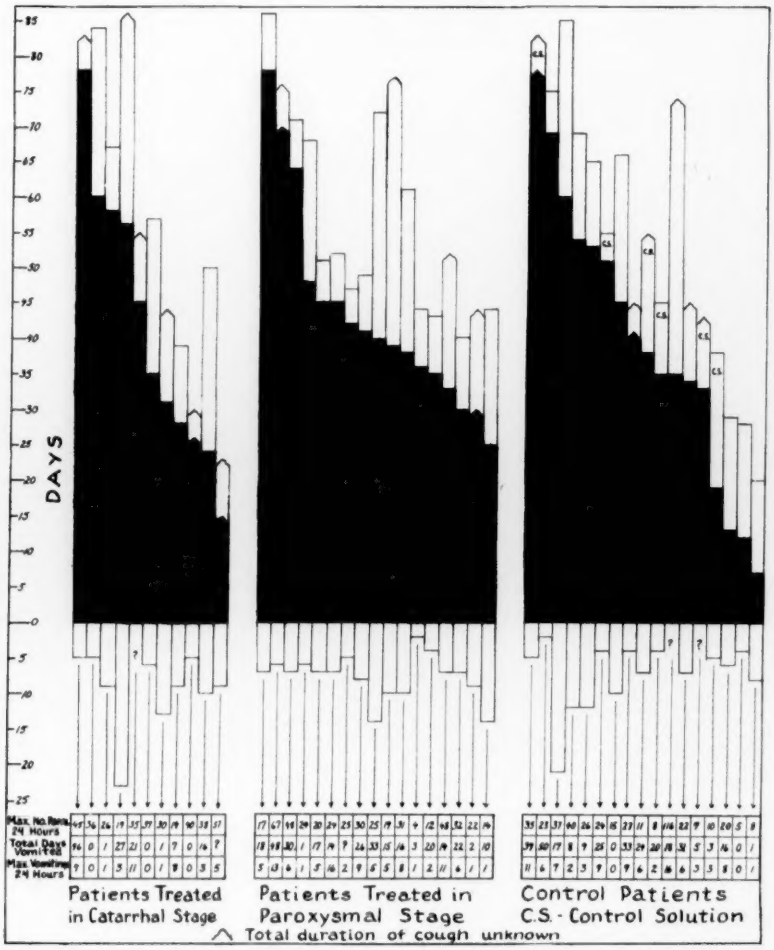
DAYS
Patients Treated in Catarrhal Stage
Patients Treated in Paroxysmal Stage
Control Patients C.S. - Control Solution
Total duration of cough unknown

Chart 9.—Chart showing the duration of the disease in the treated and the untreated patients, the maximum number of paroxysms in twenty-four hours, the total days of vomiting and the maximum number of vomitings in twenty-four hours. The solid black area indicates the duration of the paroxysmal stage. The ascending columns indicate the duration of the postparoxysmal cough. The descending columns indicate the duration of the catarrhal stage.

Luttinger [15] described treatment with vaccine as reducing the period of postparoxysmal cough. Treatment with H. pertussis undenatured bacterial antigen did not seem to do so (chart 9).

The duration of the catarrhal stage in the two groups was recorded for comparison with Lawson's epidemiologic data.[16] The mean duration of catarrh for patients treated in the catarrhal stage was nine and four-tenths days. For control patients and those who did not receive injections until after the appearance of paroxysms the mean duration was seven and five-tenths days. This difference is without significance. Lawson, in a study of 1,564 cases, found that the mean duration of the catarrhal period was ten and nine-tenths days. (The definition of paroxysm we have used, which differs from the conventional one, may account for our slightly shorter mean.) The variability of the duration of the preliminary period of catarrh confirms a previous observation.[17] The range was from two to twenty-three days (chart 9).

The duration of the paroxysmal stage in the treated and control groups is shown to be of the same order (table and chart 9). For the test group the range was from twenty-four to seventy-eight days, with a mean of forty-two days. For the control group the range was from seven to seventy-eight days, with a mean of thirty-eight days. The difference in the two means is without statistical significance. Using vaccine therapy, Luttinger [15] found that the paroxysmal stage averaged thirty-seven days, whereas the mean for his control group was fifty days.

The mean maximum number of paroxysms in twenty-four hours for each of the two groups is recorded in the table. The mean peak for the test group was thirty and for the control group twenty-five and one-half. These peaks are higher than those described by Faber and Struble and Bamberger and Menke. This is because by our definition a paroxysm, for the reasons previously mentioned, included all coughing of thirty seconds' duration or more whether the child whooped or not. The peaks attained by individual patients show a wide variation. Two thirds of all the children had a peak of from eleven to forty paroxysms. The highest number recorded for any child for twenty-four hours was one hundred and sixteen.

The day on which the peak of paroxysms occurred likewise varied a great deal. Generally, however, it occurred between the eighth and the twelfth day of the paroxysmal stage.

15. Luttinger, P.: Pertussis Vaccine, J. A. M. A. **68**:1461 (May 19) 1917.

16. Lawson, G. M.: Epidemiology of Whooping Cough, Am. J. Dis. Child. **46**:1454 (Dec.) 1933.

17. Miller, J. J., Jr.: California & West. Med. **43**:138, 1935.

The number of days of vomiting for patients in each group varied from none to about fifty. The mean number of days of vomiting was the same (fourteen) for the test and for the control group. The maximum number of vomitings in twenty-four hours varied for both groups from none to sixteen. The mean maximum for both groups was close to five.

Edema of the eyelids occurred in the majority of patients in both the test and the control group. Hemorrhages occurred in only 4 patients.

A rough clinical appraisal was made of the condition of each patient as he was seen in the home from day to day. This appraisal was made on the appearance of the child, the amount of prostration present and the severity of any coughing or vomiting which occurred during the visit. The frequency of paroxysms as recorded by the parent, which has been discussed at length, is obviously only a part of the picture. In making our clinical appraisals we tried not to give the records of the frequency of paroxysms too much weight. For example, a 5 year old boy who had a maximum of one hundred and sixteen paroxysms in twenty-four hours did not have really severe seizures. Furthermore, the seizures rapidly diminished in number, ceasing within three weeks after the peak. (Unfortunately, this dramatic decline in frequency occurred without the help of injections of any kind.) The child's condition was appraised as moderate.

On the basis of this clinical estimate the disease was mild in 2 patients of the treated group, moderate in 20 and severe in 6. It was mild in 4 patients of the control group, moderate in 9 and severe in 4. In view of the evidence cited [18] that the mortality for pertussis is higher for girls than for boys, our data were examined with regard to the comparative severity in the two sexes. Treatment with H. pertussis undenatured bacterial antigen was disregarded, since an approximately equal number of boys and of girls (15 and 13) received injections. The following criteria of severity were compared: the total duration of the paroxysmal stage, the maximum number of paroxysms in twenty-four hours, the total days of vomiting and the maximum number of vomitings in twenty-four hours. The means of these factors showed no difference of statistical significance between the sexes. By our rough clinical appraisal, we found that the disease was mild in 4 boys, moderate in 18 and severe in 6 and that it was mild in 2 girls, moderate in 11 and severe in 4.

The seasonal distribution of the disease was the same in the two groups. Treated and untreated patients were observed in three local epidemics.

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18. Luttinger.[3] Herman and Bell.[4]

COMMENT

This study was undertaken with high hopes of our being able to confirm the previous reports on the therapeutic efficacy of H. pertussis undenatured bacterial antigen. As has been mentioned, these reports were encouraging. There was some disagreement as to the optimum dose and the time of administration. A rapid decrease in the frequency and the severity of seizures occurring within a few hours of the injections was described. We desired to depict this graphically.

Data have been collected for almost two years and are here presented. They depict the extraordinary variability of the disease. No evidence confirmatory of the reports of Frawley, Stallings and Nichols and Munns and Aldrich was obtained. The small doses advised by the last four authors seemed quite valueless. No "rapid alleviation of symptoms occurring within two or three hours" was observed.

It is not possible, however, to contradict Frawley's second report,[2] in which he advises the use of doses of 5 cc. twice a day. We were not able to see our patients twice a day. We did, however, give several patients 10 cc. (5 cc. in each arm) in one visit. Single doses of 7 cc. were found to provoke considerable local reaction, whereas doses of 5 cc. did not. It may be significant that when our second lot of H. pertussis undenatured bacterial antigen, which contained twice as much protein nitrogen as the first lot (2.25 mg. per hundred cubic centimeters, rather than 1.05 mg.), was given in daily doses of from 5 cc. to 10 cc. we had our only instances of an observed decrease in frequency together with a reported decrease in severity. The duration of paroxysms in these instances, also, was slightly less than the mean duration for the children who received injections (but not less than the mean was for the control children). It is of course possible that these large doses of this particular lot benefited the children. The fact that some patients had the disease much more mildly without any injections is not contradictory to the possibility.

We are inclined to believe, however, that even large doses of H. pertussis undenatured bacterial antigen given more than once a day will not prove to be useful therapeutically. The practical difficulties of giving these injections are great. For reasons pertaining to the public health the child should remain at home. Daily house calls (not to mention calls twice a day) during an epidemic of pertussis must be productive of splendid results to be worth the cost to the parent and the physician.

There is reason also to doubt that H. pertussis undenatured bacterial antigen is an effective antigen. In children its injection is followed by the gradual appearance of antibodies—complement-fixing antibodies,

agglutinins and precipitins.[19] Opsonins are not demonstrable, however.[20] Clinical immunity is not produced. We have seen pertussis occur in 13 children who had received 10 cc. of H. pertussis undenatured bacterial antigen from six weeks to twelve months previously.

The proponents of antigen treatment are many. They outnumber the opponents. The conservative view has recently been summarized by Fothergill.[21] The only hope of settling the argument lies, we believe, in utilization of the method we have outlined. Hospitalization is probably necessary, for with it the therapeutic effect of the injection on the parents is avoided and the task of recording the frequency of paroxysms is in the hands of trained persons who are on duty twenty-four hours. Bamberger and Menke have shown how to make the records and have indeed furnished a base-line for evaluating therapeutic agents for this disease.

## SUMMARY

The course of pertussis in 45 children was observed closely in the home. Daily counts of the number of paroxysms, whoops and vomitings were made by the patients' parents. Combined subcutaneous and intradermal injections of H. pertussis undenatured bacterial antigen were given to 28 of these children. The doses used varied widely, for the doses recommended by different proponents of this form of therapy vary.

A marked decrease in the frequency of paroxysms and of vomiting was associated with these injections only occasionally. Such decreases may have been due to the treatment, but the possibility of their being chance variations seems likely.

In both the test and the control groups, marked individual variations occurred in the total duration of the disease, in the duration of the catarrhal stage, in the duration of the paroxysmal stage, in the duration of vomiting and in the maximum number of paroxysms and the maximum number of vomitings in twenty-four hours. No significant differences as judged by these criteria were found to exist between the treated and the untreated patients.

We were thus unable to confirm the previous favorable reports of the therapeutic value of H. pertussis undenatured bacterial antigen.

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19. Miller, J. J., Jr.; Browne, A. S., and McCrea, N.: Proc. Soc. Exper. Biol. & Med. **32**:299, 1934.

20. Singer-Brooks, C., and Miller, J. J., Jr.: The Opsonocytophagic Test During Pertussis and in Children Vaccinated with H. Pertussis Antigens, to be published.

21. Fothergill, L. D.: M. Clin. North America **19**:1409, 1936.

# PHYSICAL STATUS OF TWO HUNDRED AND NINETEEN PUEBLO INDIAN CHILDREN

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A study of the general physical status of 219 Pueblo Indian children who were from 7 to 11 years of age and who lived in eight pueblos or villages was made in the summer and fall of 1934. Six of the villages were in New Mexico, and two were in Arizona. The children had been the subject of anthropometric measurements for three years.[1]

The Pueblo Indians are a group of agricultural tribes living in villages in north central New Mexico and northeast Arizona. This region is located in the driest and sunniest part of the United States. The altitude is high, varying between 5,000 and 7,000 feet (1,524 and 2,134 meters); the temperature is subject to wide variations both daily and seasonally.[2]

These people live in houses built of adobe (mud cakes). The rooms are likely to be dark since windows are few. The windows and doors are, as a rule, unscreened. All the members of a family usually sleep in one room, some in beds, some on the floor. There is almost complete lack of sanitary arrangements. Water is scarce, and in many villages the entire supply is a single well.

The diet of the children is poor in quality and quantity. Milk (canned) is used only in coffee. For many children breakfast consists

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A cooperative study by the Children's Bureau of the United States Department of Labor, the Carnegie Institution of Washington and the Departments of Pediatrics and Radiology of the Yale University School of Medicine.

1. The anthropometric measurements are part of a comprehensive study of Indian children being made under the direction of Dr. Sophie D. Aberle, formerly of the Carnegie Institution of Washington and Yale University (now of the Office of Indian Affairs, United States Department of the Interior).

2. Hewett, Edgar Lee; Henderson, Junius, and Robbins, Wilfred William: The Physiography of the Rio Grande Valley, New Mexico, in Relation to Pueblo Culture, Bulletin 54, United States Bureau of American Ethnology, 1913, p. 18.

of bread and coffee and lunch of bread and jelly. The eating habits of the children are unsupervised and irregular. A child may or may not appear for a meal, and no child is required to eat anything he does not want. Very young children are often fed from the plates of the adults. In several of the day schools an apple and a cup of milk are given to each child once or twice a day.[3]

Of the 219 children studied, 103 were boys, and 116, girls. The number of children examined in the various pueblos is shown in table 1, and the age and sex of the children, in table 2.

TABLE 1.—*Number of Indian Boys and Girls in Specific Pueblos*

| State and Pueblo | Total Children | Boys | Girls |
|---|---|---|---|
| New Mexico | | | |
| San Juan | 34 | 18 | 16 |
| Santa Clara | 27 | 12 | 15 |
| Cochiti | 21 | 10 | 11 |
| San Felipe | 29 | 14 | 15 |
| Acomita | 28 | 11 | 17 |
| McCarty's | 21 | 9 | 12 |
| Arizona | | | |
| Oraibi | 31 | 14 | 17 |
| Hotevilla | 28 | 15 | 13 |
| Total | 219 | 103 | 116 |

TABLE 2.—*Age Distribution of Indian Boys and Girls*

| Age of Child | Total Children | Boys | Girls |
|---|---|---|---|
| 7 years | 16 | 9 | 7 |
| 8 years | 44 | 16 | 28 |
| 9 years | 80 | 42 | 38 |
| 10 years | 47 | 25 | 22 |
| 11 years | 25 | 8 | 17 |
| 7 to 11 years* | 7 | 3 | 4 |
| Total | 219 | 103 | 116 |

* Exact age not reported.

Physical examinations and estimates of general condition and nutritional status were made. The children were weighed, their standing heights (crown-heel lengths) were measured and their body temperatures were taken by mouth. Wassermann and tuberculin tests, blood counts, hemoglobin estimations and roentgenographic examinations of the chests and abdomens were made.

## OBSERVATIONS ON THE CHILDREN

*Body Temperature.*—The body temperatures of 214 children were taken by mouth.[4] The temperatures of 32 per cent of the children

3. The information on diet was taken from unpublished material collected by Elizabeth Pitney in connection with the study mentioned in footnote 1.

4. The temperatures were taken at varying times of day and under varying circumstances in relation to meals and other activities.

were below 99 F. and were considered normal. The temperatures of 68 per cent were 99 F. or above and were considered abnormal, although in only 8 children was the temperature 100 F. or higher.

*Height and Weight.*—The average height and weight of the Indian children studied (heights of 102 boys and 116 girls and weights of 95 boys and 114 girls) are shown for each year of age in the accompanying charts (fig. 1), together with the corresponding averages for 8,525 white boys and 8,470 white girls of the same ages reported by Collins and Clark.[5] These charts show that the average child of this Pueblo

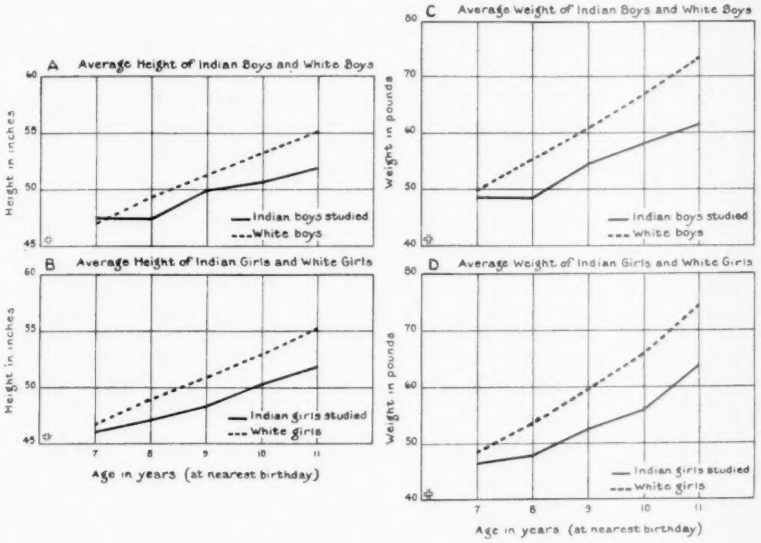
A Average Height of Indian Boys and White Boys
Height in inches
Indian boys studied
White boys
B Average Height of Indian Girls and White Girls
Height in inches
Indian girls studied
White girls
Age in years (at nearest birthday)
C Average Weight of Indian Boys and White Boys
Weight in pounds
Indian boys studied
White boys
D Average Weight of Indian Girls and White Girls
Weight in pounds
Indian girls studied
White girls
Age in years (at nearest birthday)

Fig. 1.—*A* compares the average heights of Indian boys and white boys; *B*, those of Indian girls and white girls. *C* compares the average weights of Indian boys and white boys; *D*, those of Indian girls and white girls. The white children were born in the United States of native white parents and grandparents (Collins and Clark [5]).

Indian group is shorter and lighter than the average white child of the same age and sex in the group reported.[6]

5. Collins, Selwyn D., and Clark, Taliaferro: Physical Measurements of Boys and Girls of Native White Race Stock (Third Generation Native Born) in the United States, Pub. Health Rep. **44**:1066 (May 3) 1929.

6. Nearly 30,000 school children from 6 to 15 years of age who were born of native white parents and grandparents living in various sections of the United States were studied by Collins and Clark; of these, only children from 7 to 11 years of age are represented in figure 1.

Steggerda,[7] of the Carnegie Institution of Washington, determined the average height and weight of 715 Navaho Indian boys and 634 Navaho Indian girls from 7 to 11 years of age. When the average height of these children was compared with that of the white and of the Pueblo Indian boys and girls shown in figure 1, it was found to be about the same as that of the white but above that of the Pueblo Indian boys and girls. The average weight, however, of the Navaho Indian boys and girls was found to be below that of the white but, as in the case of height, above that of the Pueblo Indian boys and girls.

*Nutritional Status.*—Estimations of the general nutritional status were based on clinical judgments of the amount of subcutaneous fat, the tone and development of the muscles and the color of the mucous membranes.

The amount of subcutaneous fat was considered "good" in 22 per cent of 217 children examined, "fair" in 41 per cent and "poor" in 38 per cent. On the basis of clinical estimations 6 children were considered "obese," and 81 "malnourished." The musculature was considered "good" in 18 per cent, "fair" in 47 per cent and "poor" in 35 per cent. The color of the mucous membranes was considered "good" in 97 per cent of 184 children examined and "poor" in 3 per cent.

On the basis of these observations the general nutritional condition was estimated to be "good" in 17 per cent of the 167 cases in which all three items were recorded, "fair" in 48 per cent and "poor" in 34 per cent.

*Posture.*—The posture was recorded as "good" in 6 per cent of 215 children examined, "fair" in 50 per cent and "poor" in 44 per cent. The most frequent postural defects were "winged" scapulae, pot belly and lordosis; less frequent were scoliosis and relaxation of joints and tendons. Lateral curving of the thighs and lower parts of the legs was common, occurring in more than two thirds of those examined, but anterposterior bowing of the legs and thighs and bowing of the lower ends of the tibias and fibulas, such as are found in rickets, were relatively rare. Knock-knee was extremely common, occurring in 90 per cent of the 217 children examined.

*Other Findings.*—The teeth of the children were examined for the presence of caries, which was found in temporary or permanent teeth in 86 per cent of 216 children examined. Ninety-seven of them had from one to three carious teeth; 89 had four or more. One or more alveolar abscesses were found in the teeth of 12 per cent.

7. The data given were taken from an unpublished study, "Height, Weight and Age Tables for Homogeneous Groups, with Particular Reference to Navaho Indians and Dutch Whites," by Morris Steggerda and Paul Densen of the Carnegie Institution of Washington.

The tonsils were recorded as enlarged in 86 (40 per cent) of 217 children examined. Tonsillitis, acute or chronic, was found in 15 of the 86 children whose tonsils were enlarged. Tonsillitis was found in 13 additional children whose tonsils were not recorded as enlarged. The adenoids were found enlarged in 28 per cent of 211 children examined.

Sixty (28 per cent) of 215 children examined showed enlargement of the cervical lymph nodes, the tonsillar nodes alone being involved in 26 of the 60 cases. Acute inflammation or suppuration was not present in any case.

The thyroid gland was definitely enlarged in 15 per cent of 212 children examined, and the isthmus was palpable in 178 (96 per cent) of 186 children. No child with exophthalmic goiter was observed, and in only 1 child was tachycardia found.

Congenital defects were rare, being found in only 8 of 217 children examined. Deformity of the elbow or elbows, accessory teeth and cleft uvula occurred twice each; dislocation of the hip and malformation of the heart, once each.

*Results of Examination of the Blood.*—Anemia was found on clinical examination in only 2 of the 217 children examined. That it actually occurred more frequently is shown by the fact that 17 per cent of the red blood cell counts for 199 children were below normal limits. Of the hemoglobin estimations[8] for 192 children, 24 (13 per cent) were below normal limits. There was a high incidence of polycythemia (52 per cent), which can probably be explained by the high altitude at which the children live. The white blood cell count was within normal limits in 68 per cent of 200 children, above in 20 per cent and below in 13 per cent. Differential blood cell counts made for 192 children showed that more than two thirds of the counts were within normal limits. In 22 per cent there was definite eosinophilia, the percentage of eosinophils varying from 6 to 22. Since infections of the skin were found to be relatively uncommon among these children, intestinal parasitic infestation probably played a rôle in producing the eosinophilia, but this cannot be proved, as examinations of the stools were not made.

*Evidence of Infection on Clinical Examination.*—Examination of the eyes was made with particular care because of the well known prevalence of trachoma among Indians. Conjunctivitis of a nonspecific nature was found in 50 per cent of the 217 children examined. In these cases there was reddening limited to the palpebral conjunctivae, without discharge or photophobia. The etiology is not known, but the continual bright sunlight in the region may, of course, be a factor. In

8. Readings were made with a Haden-Hauser hemoglobinometer.

some cases the conjunctivitis was severe and was difficult to differentiate from trachoma. Trachoma was found in 14 per cent of 217 children, an incidence which is comparable to that of 11 per cent reported by Warner [9] for 375 children attending day school on reservations in this area. There was, moreover, in the present study an additional 9 per cent of children in whom the presence of trachoma was suspected, but in whom it could not be definitely diagnosed.

Evidences of respiratory tract infections were found in only 34 (16 per cent) of 217 children examined. The most frequent condition was rhinitis. Bronchitis, suppurative otitis media, pharyngitis and sinusitis occurred once each. Pulmonary tuberculosis, although suspected in 2 children, was not definitely diagnosed on clinical examination in any case.

*Infections of the Skin.*—Infections of the skin, said to be common among Indians, were found in only 10 per cent of 217 children examined; in more than half of the cases a diagnosis of impetigo was made.

Of the 217 children given clinical examinations, only 1 showed signs of syphilis. This finding was confirmed by a Wassermann test. In another child the existence of syphilis was suspected because of hypoplasia of the upper middle incisors and apparent mental retardation, but a Wassermann test was not made. Wassermann tests were made in 190 cases and gave a positive reaction in 4, showing an incidence of syphilis of 2 per cent. Hancock [10] found in a "Wassermann survey" of 427 Navaho Indian children an incidence of syphilis of 7.2 per cent.

*Tuberculosis—Roentgenographic and Laboratory Findings.*—In addition to the clinical examinations for tuberculosis mentioned previously, intradermal tuberculin tests were given, and roentgenographic examinations of the chest and abdomen were made.

Of the 206 children who were given the tuberculin test,[11] 30 per cent reacted positively and 51 per cent negatively; in 19 per cent the results of the tests were questionable. It would, of course, have been desirable to repeat the tests with a stronger dose of tuberculin, but for

9. Warner, H. J.: Notes on the Results of Trachoma Work by the Indian Service in Arizona and New Mexico, Pub. Health Rep. **44**:2913 (Nov. 29) 1929.

10. Hancock, J. C.: Diseases Among the Indians, Southwestern Med. **17**: 126 (April) 1933.

11. The old tuberculin used was obtained from the laboratory of the Trudo Sanatorium, New York, marked strain H61, and was diluted in the New Haven Hospital clinic with sterile salt solution so that 0.1 cc. of the solution contained 0.01 mg. of old tuberculin.

various reasons this was not possible. No reports of tuberculin tests previously made among Pueblo Indian children have been found. Reports of such tests made among Indian children of other tribes are not comparable, since the same dose of tuberculin, namely, 0.01 mg. of old tuberculin, was not used. However, Hetherington and his co-workers,[12] using this dose of old tuberculin, found that in Philadelphia 36 per cent of 1,236 white and colored children of the same age group as these Pueblo Indian children reacted positively. This is not a significantly higher incidence than was found among the children in the present study (30 per cent).

Routine roentgenographic examinations[13] of the chest were made one to two months after the other examinations were completed. For

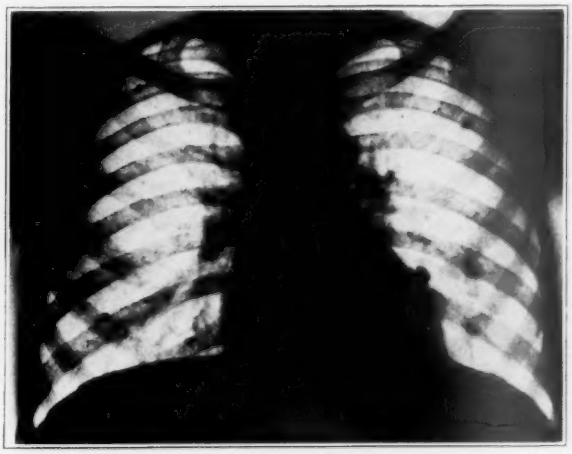

Fig. 2.—Roentgenogram of the chest of an Indian child with calcified lymph nodes in the hilar region and in the parenchyma.

the purpose of taking the roentgenograms the children were transported to the Indian Tuberculosis Sanatorium in Albuquerque, N. M., and the Indian Service Hospital at Keams Canyon, Ariz. Readings of

12. Hetherington, H. W.; McPhedran, F. Maurice; Landis, H. R. M., and Opie, Eugene L.: A Survey to Determine the Prevalence of Tuberculous Infection in School Children, Am. Rev. Tuberc. **20**:421 (Oct.) 1929.

13. The technical factors for taking the roentgenograms of the chest were: kilovolt power 76, milliamperes 100, target-film distance 72 inches and time one-tenth second. Those for taking the roentgenograms of the abdomen were kilovolt power 73, milliamperes 10, target-film distance (centering midway between the iliac crest and the costal margin) 30 inches and time one-half second. The children were placed in the erect position for taking the roentgenograms of the chest and in the prone position for taking those of the abdomen.

the films [14] were done without reference to the clinical findings or the results of the tuberculin tests. Notation was made of any abnormalities, including the presence of calcium, fibrosis, infiltration, and pleural and mediastinal changes.

Films of the chests of 183 children were examined for evidence of deposits of calcium in lymph nodes. Only nodelike areas which were dense and had sharply defined edges were regarded as evidence of deposits of calcium. Evidence of calcium was seen in 42 (23 per cent) of the films. In half of the cases the calcified nodes were found in the hilar region only. In the other half such nodes were found in the parenchyma of the lung (Ghon tubercles), and in 4 of these cases the calcified nodes were found in the hilar region also. Figure 2 shows a roentgenogram of the chest of an Indian child, in whom many lymph nodes were calcified in both the hilar region and the parenchyma. Of the

TABLE 3.—*Result of Tuberculin Test in Relation to Calcium as Shown by Roentgenograms of Chests of Indian Children*

| Result of Tuberculin Test | Total Children | Calcium in Chest | | | | |
|---|---|---|---|---|---|---|
| | | Total Reported | Positive | Questionable | Negative | Not Reported |
| Result of tuberculin test reported | 206 | 173 | 40 | 47 | 86 | 33 |
| Positive | 62 | 54 | 25 | 14 | 15 | 8 |
| Questionable | 41 | 33 | 8 | 8 | 17 | 8 |
| Negative | 103 | 86 | 7 | 25 | 54 | 17 |
| Result of tuberculin test not reported | 13 | 10 | 2 | 2 | 6 | 3 |
| Total children | 219 | 183 | 42 | 49 | 92 | 36 |

children in whom calcification of lymph nodes occurred, two thirds were girls and one third boys. In an additional 49 (27 per cent) of the 183 children the presence of calcium was suspected but could not be definitely determined; in 92 (50 per cent) of the films no calcium was shown.

The results of the tuberculin tests in relation to the roentgenographic observations for the 219 children are shown in table 3. There were 25 children for whom both the tuberculin test and the roentgenographic observations indicated the presence of tuberculosis. In 15 children the tuberculin test gave a positive result, and the roentgenographic examination, a negative result; in 14 the tuberculin test gave a positive reaction, and the roentgenographic evidence was questionable, and in 8 there was a positive reaction to the tuberculin test, and the roentgenographic observations were not reported. In 7 children there was roentgeno-

14. Miriam E. Brailey, M.D., director of the Harriet Lane Tuberculosis Clinic of the Johns Hopkins Hospital and instructor in epidemiology in the School of Hygiene and Public Health of Johns Hopkins University, gave valuable assistance in interpretation of the films of the chest.

graphic evidence of tuberculosis, and the tuberculin test gave a negative result; in 8 the roentgenograms showed a tuberculous condition, and the result of the tuberculin test was questionable; in 2 the roentgenographic evidence indicated the presence of tuberculosis, and the result of the tuberculin test was not reported. Altogether there were 79 children in whom there was roentgenographic evidence of calcification of the lymph nodes, in whom a positive reaction to the tuberculin test occurred or in whom both these types of observations showed that tuberculosis was present. Thus the incidence of infection with tuberculosis was 36 per cent (79 of 219 children).

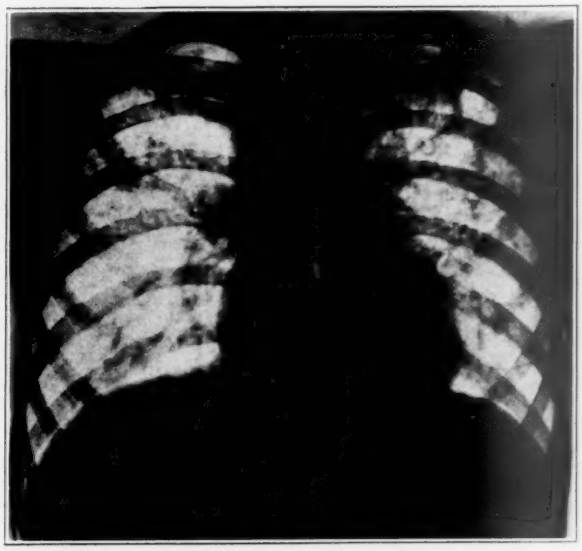

Fig. 3.—Roentgenogram of the chest of an Indian child with a generalized tuberculous process of adult type.

The pulmonary fields were examined for parenchymal changes, with or without evidences of deposits of calcium. As already pointed out in the discussion of infections of the respiratory tract, in no case was a clinical diagnosis of pulmonary tuberculosis definitely made. From the roentgenogram alone a diagnosis of pulmonary tuberculosis was made in only 4 instances. In 1 of these there was a generalized tuberculous process of the adult type (fig. 3), and in another, pulmonary infiltration of the childhood type; in both, the primary calcified nodes (Ghon tubercles) were present. In the third case there was fibrosis of the right apex with calcium deposits in the tracheobronchial lymph nodes, and in the fourth the childhood type of pulmonary tuberculosis was diagnosed in the absence of calcium. In the first and third of

these cases the intradermal tuberculin test gave a positive result, in the second the test was not made, and in the fourth it gave a negative result. There were 5 additional cases in which pulmonary tuberculosis was suspected, but in none of these was calcium present in the lymph nodes or the parenchyma. In 2 of these the result of the tuberculin test was positive, and in 3 it was negative. In no case, however, in which pulmonary tuberculosis had been diagnosed on roentgenographic examination or even suspected to exist were signs found on clinical examination of the child's lungs.

The cervical region was visible in the roentgenograms of the chests of 126 children. In no instance was any definite evidence of calcification of the lymph nodes of this region found.

Satisfactory roentgenograms of the abdomen were taken for 179 children. In only 1 were any deposits of calcium seen in the lymph nodes.

*Other Roentgenographic Findings.*—The cardiac silhouette was observed as part of the examination of the roentgenograms of the chest, even though special technic had not been used for the purpose of studying it. In 1 case only did the roentgenograms show any abnormality of the heart—this was an enlargement. In the 1 instance in which clinical diagnosis was made of an abnormality of the heart (congenital abnormality) the cardiac silhouette was considered normal.

The parts of the skeleton visible in the roentgenograms of the chest and abdomen also were examined for abnormalities. Very few pathologic conditions were found. Markedly increased calcification of the vertebral epiphyses was noted in 1 film, and general decalcification of vertebrae in 1; the significance of these findings was not apparent. A clinical diagnosis of congenital dislocation of the hip was confirmed. A number of other congenital defects were found, none of which was associated with any symptoms or clinical signs. Spina bifida was found in the roentgenograms of 55 per cent of 178 children. That this is not an unusual finding is shown by the fact that in 1935 Karlin[15] reported that he found spina bifida in 27 (54 per cent) routine roentgenograms of the spines of a group of 50 children with no clinical evidence of this defect.

## SUMMARY AND COMMENTS

A study has been made of the general physical status of 219 Pueblo Indian children from 7 to 11 years of age.

When the average heights and weights of these children were compared with those of a large group of white children and a smaller number of Navaho Indian children, it was found that the Pueblo Indian

15. Karlin, I. W.: Incidence of Spina Bifida Occulta in Children With and Without Enuresis, Am. J. Dis. Child. **49**:125 (Jan.) 1935.

children were shorter and lighter for their age than either white or Navaho Indian children of the same age and sex.

The nutritional status, judged by the amount of subcutaneous fat, the musculature and the color of the mucous membranes, was considered "poor" in more than one third of the children, "fair" in nearly one half and "good" in only one sixth.

The posture was considered "poor" in 44 per cent of the children and "fair" in 50 per cent. In only 6 per cent was the posture classified as "good."

Caries of one or more of the teeth was found in 86 per cent of the children and alveolar abscesses, in 12 per cent. Enlarged tonsils or adenoids were found in about one third of the children. The thyroid gland was enlarged in 15 per cent of the children, but in no case was any evidence of exophthalmic goiter found.

The red blood cell counts were below normal in only 17 per cent of the children; in 52 per cent, however, there was polycythemia. In 68 per cent of the children the white blood cell counts were within normal limits. The only important finding from differential blood cell counts was a definite eosinophilia in 22 per cent of the children.

Trachoma was found in 14 per cent of the children, and its presence was suspected in an additional 9 per cent.

Evidences of infection of the skin were present in 10 per cent of the children.

The incidence of syphilis was 2 per cent.

Infection of the respiratory tract was found in 16 per cent of the children.

Roentgenographic examinations of the chest showed evidence of calcification of the lymph nodes in 23 per cent of the children.

The incidence of infection with tuberculosis, based on the outcome of tuberculin tests or of roentgenographic examinations of the chest or on both these criteria, was 36 per cent (79 of 219 children).

Clinical examinations of these children should be repeated in order to evaluate more accurately the findings at this first examination. The tuberculin tests should be repeated, with stronger doses of tuberculin, and roentgenograms be made of the lungs of children who react positively to the stronger doses. Additional roentgenograms should be taken of the children whose roentgenograms at the first examination showed positive evidence of tuberculosis. The stools of all these children should be examined for parasites. It is obvious that this report is preliminary in character. The work merely serves as a basis for further studies.

Mr. John Collier, United States Commissioner of Indian Affairs, made this study possible, and members of his staff cooperated in it.

# USE OF CONVALESCENT SERUM IN THE PREVENTION OF CHICKENPOX

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Chickenpox is usually a mild disease, and therefore no attempt is made in private practice to prevent its development in exposed persons. On the other hand, the presence of chickenpox in children's institutions and hospitals warrants the use of any procedure which may prevent the spread of the disease, as successive outbreaks may bring about a quarantine for months.

In 1923 Blackfan, Peterson and Conroy [1] reported favorable results with the use of convalescent serum in the prevention of chickenpox. Forty-two susceptible children exposed five days previously were given 5 cc. of convalescent serum. Only seven of these children subsequently had chickenpox, and in every instance the disease was mild.

In 1924 Weech [2] also reported favorable results with the employment of convalescent serum as a preventive agent. Of nine infants receiving from 3 to 4.5 cc. of convalescent serum from one to six days after exposure to chickenpox, eight did not contract the disease; the exception was an infant who had mild chickenpox.

Later Mitchell and Ravenel,[3] von Barabas,[4] Greenthal[5] and Gordon and Meader,[6] among others, published reports extolling the value of convalescent serum in the prophylaxis of varicella. Gordon and Meader emphasized the importance of collecting the serum within one month

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From the Home for Hebrew Infants.

1. Blackfan, K. D.; Peterson, M. F., and Conroy, F. C.: Use of Convalescent Serum as a Prophylaxis in Measles and Chicken Pox, Ohio State M. J. **19**:97 (Feb.) 1923.

2. Weech, A. A.: The Prophylaxis of Varicella with Convalescents' Serum, J. A. M. A. **82**:1245 (April 19) 1924.

3. Mitchell, A. G., and Ravenel, S. J.: The Value of Convalescent Serum in Protection Against Varicella, Arch. Pediat. **42**:709, 1925.

4. von Barabas, Z.: Prophylaxis of Chicken Pox by Convalescent Serum, Jahrb. f. Kinderh. **107**:343 (June) 1925.

5. Greenthal, R. M.: Chicken Pox and Whooping Cough: Prevention and Treatment, Wisconsin M. J. **27**:540 (Dec.) 1928.

6. Gordon, J. E., and Meader, F. M.: The Period of Infectivity and Serum Prevention of Chicken Pox, J. A. M. A. **93**:2013 (Dec. 28) 1929.

of the period of the eruption and stated that if it were collected after five months protection was furnished only one third of the inoculated patients.

Lately Kereszturi, Hauptman and Park [7] reported that convalescent serum was of no value in the prevention of chickenpox. It is interesting to note, however, that these investigators employed a serum collected from persons who had had chickenpox nine months previously, so that the question arises whether this serum should be regarded as convalescent serum.

During the spring of 1936, chickenpox developed in children in the Home for Hebrew Infants, and in view of the many favorable reports regarding the use of convalescent serum in the prevention of varicella, it was decided to employ that agent with the hope of checking the outbreak. At the same time it was felt that with the employment of control groups of cases one would be in a good position to evaluate the efficacy of this procedure. It should be emphasized that in most of the articles praising the value of convalescent serum in chickenpox no control cases had been reported, so that one might inquire whether the favorable results were mere coincidence. It is of interest that when a child had chickenpox in the infirmary, which contains twenty-three individual glass cubicles, most of the remaining patients did not contract the disease. The children in the infirmary are kept in bed and therefore are not in direct contact with one another.

The convalescent serum which we used at the beginning of the outbreak was obtained from twenty children two weeks after the onset of chickenpox. This serum was pooled, and 10 cc. was inoculated intragluteally into seventeen children exposed to chickenpox in wards 2, 6 and 9. Nineteen children of the same wards did not receive any inoculations and served as controls. There are no partitions in these wards, and the children come into intimate contact with one another.

The treated children in wards 2 and 6 received convalescent serum one day after exposure to chickenpox, and those in ward 9 received the serum on the same day that exposure occurred.

As will be noted in tables 1 and 2, of the seventeen children receiving convalescent serum, fifteen later had chickenpox, and of the nineteen untreated children eighteen contracted the disease. The fact that chickenpox developed in the treated group from twelve to seventeen days after the inoculation of serum indicates that the injection was given either immediately prior to the incubation period or within the first few days of that period.

7. Kereszturi, C.; Hauptman, D., and Park, W. H.: Value of Convalescent Serum for Prevention of Common Contagious Diseases of Children, Am. J. Dis. Child. **50**:309 (Aug.) 1935.

It may be recalled that we used convalescent serum obtained from children two weeks after the initial appearance of the rash. The question arose whether immune substances make their appearance in

TABLE 1.—*Clinical Data on Children Receiving 10 Cc. of Convalescent Serum After Having Been Exposed to Chickenpox*

| Case | Age Yr. | Age Mo. | Ward | Date of First Day of Exposure to Chickenpox | Date of Administration of Convalescent Serum | Date of Onset of Chickenpox | Interval Between Inoculation and Onset of Disease Days | Course of Disease |
|---|---|---|---|---|---|---|---|---|
| S. D. | 2 | 11 | 6 | 3/28 | 3/29 | 4/13 | 15 | Mild |
| R. S. | 2 | 3 | 6 | 3/28 | 3/29 | 4/13 | 15 | Moderate |
| H. S. | 3 | 4 | 6 | 3/28 | 3/29 | 4/13 | 15 | Moderate |
| A. N. | 2 | 3 | 6 | 3/28 | 3/29 | 4/10 | 12 | Mild |
| E. A. | 2 | 11 | 6 | 3/28 | 3/29 | .... | .. | ..... |
| D. R. | 2 | 5 | 2 | 3/28 | 3/29 | 4/14 | 16 | Mild |
| S. K. | 3 | 2 | 2 | 3/28 | 3/29 | 4/13 | 15 | Moderate |
| G. R. | 3 | .. | 2 | 3/28 | 3/29 | 4/11 | 13 | Moderate |
| J. W. | 2 | 9 | 2 | 3/28 | 3/29 | 4/14 | 16 | Moderate |
| L. G. | 3 | 1 | 2 | 3/28 | 3/29 | 4/13 | 15 | Mild |
| J. W. | 2 | 10 | 2 | 3/28 | 3/29 | 4/11 | 13 | Severe |
| R. K. | 3 | 4 | 2 | 3/28 | 3/29 | 4/11 | 13 | Moderate |
| S. P. | 3 | 4 | 2 | 3/28 | 3/29 | .... | .. | ..... |
| G. S. | 2 | 11 | 9 | 3/30 | 3/30 | 4/16 | 17 | Moderate |
| M. C. | 3 | 6 | 9 | 3/30 | 3/30 | 4/16 | 17 | Moderate |
| H. H. | 2 | 11 | 9 | 3/30 | 3/30 | 4/15 | 16 | Moderate |
| R. K. | 3 | .. | 9 | 3/30 | 3/30 | 4/12 | 13 | Mild |
| F. F. | 1 | .. | 5 | 4/11 | 4/14 | 4/27 | 13 | Moderate |
| B. J. | 1 | .. | 5 | 4/11 | 4/14 | 4/24 | 10 | Severe |
| E. S. | 1 | .. | 5 | 4/11 | 4/14 | 4/29 | 15 | Severe |
| F. K. | 1 | 2 | 5 | 4/11 | 4/14 | 4/29 | 15 | Mild |
| G. S. | 1 | 2 | 5 | 4/11 | 4/14 | 4/28 | 14 | Moderate |
| M. S. | 1 | .. | 5 | 4/11 | 4/14 | 4/24 | 10 | Moderate |

TABLE 2.—*Clinical Data on Children Who Did Not Receive Convalescent Serum After Having Been Exposed to Chickenpox*

| Case | Age Yr. | Age Mo. | Ward | Date of First Day of Exposure to Chickenpox | Date of Onset of Chickenpox | Course of Disease |
|---|---|---|---|---|---|---|
| I. W. | 2 | 8 | 6 | 3/28 | 4/13 | Moderate |
| R. F. | 3 | 2 | 6 | 3/28 | 4/12 | Moderate |
| A. W. | 3 | 2 | 6 | 3/28 | 4/13 | Mild |
| P. S. | 2 | 10 | 6 | 3/28 | 4/26 | Mild |
| S. C. | 2 | 4 | 6 | 3/28 | 4/12 | Moderate |
| S. B. | 2 | 6 | 6 | 3/28 | 4/16 | Mild |
| J. B. | 1 | 11 | 6 | 3/28 | 4/12 | Moderate |
| L. R. | 2 | 9 | 2 | 3/28 | 4/11 | Severe |
| R. C. | 2 | 7 | 2 | 3/28 | 4/12 | Mild |
| N. A. | 1 | 7 | 2 | 3/28 | 4/14 | Moderate |
| J. H. | 2 | 7 | 2 | 3/28 | 4/10 | Mild |
| L. W. | 1 | 11 | 2 | 3/28 | 4/11 | Severe |
| H. W. | 2 | 10 | 2 | 3/28 | 4/11 | Mild |
| E. G. | 3 | .. | 2 | 3/28 | .... | ..... |
| M. R. | 2 | 4 | 9 | 3/30 | 4/12 | Mild |
| L. R. | 2 | 9 | 9 | 3/30 | 4/11 | Mild |
| S. S. | 2 | 2 | 9 | 3/30 | 4/14 | Moderate |
| J. R. | 3 | 2 | 9 | 3/30 | 4/13 | Moderate |
| M. S. | 1 | 9 | 9 | 3/30 | 4/16 | Moderate |

the blood somewhat later than two weeks after the onset of chickenpox and whether the failure to protect the inoculated children may have been due to the employment of serum obtained too soon after an attack of the disease. In order to test the validity of this hypothesis convalescent serum was collected from ten children five weeks after the beginning

of the eruptive stage, and 10 cc. of the pooled serum was inoculated into six children exposed for three days to chickenpox in ward 5. The results of this experiment were as disappointing as those observed after the use of serum obtained at an earlier stage in the convalescent period. All six children manifested chickenpox from ten to fifteen days after the inoculation of serum.

Table 3 is a compilation of the results obtained in wards 2, 6, 9 and 5. As may be seen, 95 per cent of the untreated children and 91 per cent of the treated children had chickenpox. The percentage of mild attacks was somewhat higher in the untreated group, 44 per cent, as compared to 29 per cent in the treated group.

The failure of convalescent serum to protect against chickenpox is of interest also on account of the widespread impression that the serum of persons convalescing from diseases which result in permanent immunity contain an appreciable amount of antibodies. This idea was

TABLE 3.—*Comparison of the Incidence and Severity of Chickenpox Between Children Receiving and Those Not Receiving Convalescent Serum*

| Group | Total Number of Children | Children Having Chickenpox | | Course of Disease | | | Percentage of Mild Attacks | Percentage of Severe Attacks |
|---|---|---|---|---|---|---|---|---|
| | | Number | Percentage | Mild | Moderate | Severe | | |
| Children receiving convalescent serum..... | 23 | 21 | 91 | 6 | 12 | 3 | 29 | 14 |
| Children not receiving convalescent serum..... | 19 | 18 | 95 | 8 | 8 | 2 | 44 | 11 |

supported by the beneficial results which had been obtained with the use of convalescent serum in protecting against measles, mumps and scarlet fever. It is apparent from our experience with chickenpox that the value of convalescent serum in the prevention of a disease cannot be assumed by analogy to other diseases but must be determined by controlled investigation in the clinic.

## SUMMARY

Ten cubic centimeters of pooled convalescent serum was inoculated into twenty-three children exposed to chickenpox from one to three days previously. Nineteen children who had been exposed to chickenpox in the same wards received no inoculations and served as controls. Twenty-one children, or 91 per cent, of the treated group, contracted chickenpox; in the untreated group eighteen children, or 95 per cent, had the disease. It was somewhat more severe in the children receiving convalescent serum than in those not receiving serum. Convalescent serum therefore proved to be of no value in the prevention or mitigation of chickenpox.

# COMPARISON OF THE ANTIRACHITIC EFFECTS ON HUMAN BEINGS OF VITAMIN D FROM DIFFERENT SOURCES

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Shortly after the discovery of the production of vitamin D by the irradiation of ergosterol, the observation was made that the antirachitic effect on chickens of the irradiated ergosterol differed markedly from that of cod liver oil, rat unit for rat unit of vitamin D.[1] This raised the question of the relative efficacy in human beings of the various

TABLE 1.—*Potency of Various Vitamin D Products Commonly Used*

| Product | Daily Amount Usually Prescribed | Approximate No. of U. S. P. Units of Vitamin D |
|---|---|---|
| Cod liver oil | 3 tsp. | 1,000 |
| Viosterol | 10 drops | 2,000 |
| 10 D cod liver oil* | 1 tsp. | 1,500 |
| Halibut liver oil | 1 tsp. | 3,000 |
| Halibut liver oil and viosterol | 10 drops | 2,000 |
| Percomorph liver oil | 10 drops | 2,000 |
| Cod liver oil and percomorph liver oil | 1 tsp. | 3,100 |
| Irradiated fresh milk | 12-40 oz. | 57-190 |
| Irradiated evaporated milk | 6-20 oz. | 60-196 |

* A mixture of cod liver oil and viosterol.

vitamin D-containing substances and the dosage of each necessary for the prevention and cure of infantile rickets. For some years it has been customary to administer daily for the prevention of rickets 3 teaspoonfuls of cod liver oil, which amount contains approximately 1,000 U. S. P. units of vitamin D, or 10 drops of standard viosterol (10,000 U. S. P. [international] units of vitamin D per gram), which dose contains approximately 2,000 units. In table 1 are given most of the commonly used vitamin D products, with the number of U. S. P. units contained in the daily amount usually administered for the prevention of infantile rickets. This paper is a presentation of observations on the antirachitic

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1. Hess, A. F., and Supplee, G. C.: Proc. Soc. Exper. Biol. & Med. **27**: 609, 1930. Massengale, O. N., and Nussmeier, M.: J. Biol. Chem. **87**:423, 1930. Mussehl, F. E., and Ackerson, C. W.: Poultry Sc. **9**:334, 1930.

TABLE 2.—*Development of Rickets in Infants, Aged 13 Months and Younger, Who Received Different Amounts of Vitamin D in Various Forms Throughout Five Winter Months*

| Year of Observation | Source of Vitamin D | No. of U. S. P. Units of Vitamin D Given Daily | No. of Infants | Age, Months | | | | | | | | | Percentage of Infants | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Less Than 1 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | Maximum Degree of Rickets Subsequent to Initial Examination | | | | Actively Advancing Rickets with No Evidence of Healing at End of Period of Observation |
| | | | | | | | | | | | | | None | Extremely Slight | Mild | Moderate and Marked | |
| 1933-34 | 1 teaspoonful cod liver oil | 350 | 42 | 0 | 1 | 8 | 5 | 4 | 8 | 3 | 10 | 3 | 81 | 12 | 7 | 0 | 0 |
| 1933-34 | 2 teaspoonfuls cod liver oil | 700 | 45 | 0 | 2 | 5 | 8 | 10 | 4 | 7 | 8 | 1 | 75 | 16 | 7 | 2 | 2 |
| 1933-34 | 3 teaspoonfuls cod liver oil | 1,050 | 50 | 0 | 7 | 5 | 5 | 6 | 9 | 6 | 10 | 2 | 74 | 14 | 8 | 4 | 4 |
| 1933-34 | 1¼ drops viosterol | 270 | 50 | 0 | 9 | 10 | 11 | 4 | 3 | 8 | 3 | 2 | 82 | 16 | 2 | 0 | 0 |
| 1933-34 | 2½ drops viosterol | 540 | 44 | 1 | 10 | 8 | 10 | 3 | 5 | 2 | 5 | 0 | 68 | 25 | 7 | 0 | 2 |
| 1933-34 | 5 drops viosterol | 1,080 | 46 | 0 | 12 | 13 | 2 | 6 | 9 | 1 | 1 | 2 | 78 | 20 | 2 | 0 | 2 |
| 1933-34 | 10 drops viosterol | 2,160 | 46 | 1 | 5 | 13 | 7 | 8 | 4 | 4 | 3 | 1 | 76 | 17 | 7 | 0 | 4 |
| 1933-34 | 20 ounces (592 cc.) irradiated fresh milk | 95 | 71 | 0 | 8 | 16 | 14 | 8 | 8 | 8 | 7 | 2 | 69 | 23 | 8 | 0 | 3 |
| 1933-34 | 20-40 ounces (592-1,184 cc.) irradiated fresh milk | 95-190 | 70 | 0 | 0 | 5 | 4 | 13 | 16 | 12 | 11 | 9 | 81 | 16 | 3 | 0 | 0 |
| 1933-34 | No vitamin D | 0 | 65 | 1 | 13 | 10 | 7 | 10 | 9 | 9 | 5 | 1 | 55 | 22 | 15 | 8 | 18 |
| 1934-35 | 10-40 ounces (296-1,184 cc.) irradiated fresh milk | 47-190 | 102 | 0 | 8 | 14 | 17 | 29 | 21 | 13 | 0 | 0 | 75 | 13 | 12 | 0 | 0 |
| 1934-35 | 6-20 ounces (177.6-592 cc.) irradiated evaporated milk | 60-196 | 103 | 0 | 19 | 20 | 24 | 17 | 19 | 4 | 0 | 0 | 64 | 19 | 17 | 0 | 0 |
| 1934-35 | No vitamin D | 0 | 104 | 1 | 19 | 22 | 30 | 16 | 13 | 3 | 0 | 0 | 47 | 10 | 27 | 16 | 16 |
| 1935-36 | Irradiated yeast | 500 | 69 | 0 | 0 | 0 | 0 | 13 | 27 | 23 | 6 | 0 | 87 | 4 | 9 | 0 | 0 |
| 1935-36 | 0.43 teaspoonful cod liver oil | 150 | 74 | 0 | 13 | 21 | 13 | 17 | 6 | 4 | 0 | 0 | 69 | 19 | 12 | 0 | 3 |
| 1935-36 | 0.75 drops percomorph liver oils | 150 | 59 | 0 | 7 | 11 | 8 | 12 | 11 | 8 | 1 | 1 | 75 | 15 | 10 | 0 | 2 |
| 1935-36 | Irradiated cholesterol | 150 | 77 | 0 | 15 | 12 | 21 | 17 | 10 | 2 | 0 | 0 | 82 | 8 | 10 | 0 | 1 |
| 1935-36 | No vitamin D | 0 | 75 | 1 | 12 | 19 | 18 | 16 | 7 | 2 | 0 | 0 | 51 | 16 | 20 | 13 | 31 |

value of various amounts of cod liver oil, viosterol, irradiated fresh milk, irradiated evaporated milk, irradiated cholesterol, irradiated yeast and a mixture of fish liver oils of high potency.

## PROCEDURE

Observations were conducted during the winter months of the past three years, commencing in October or November and continuing until March or April—in every case a total of five months. Twelve hundred and twenty-eight infants were observed. These babies represented a cross-section of the infant population of Toronto. They were practically all of British and northern European stock. With the exception of some of those seen during the first winter,[2] all the infants were artificially fed with dilutions of cow's milk and added carbohydrate. The antirachitic substances used and the number of U. S. P. units of vitamin D administered daily, together with the ages of the infants at the time of the initial observation, are given in table 2. The presence or absence of

TABLE 3.—*Development of Rickets in Infants Who Received No Vitamin D Throughout Five Winter Months*

| | | Percentage of Infants | | | | |
|---|---|---|---|---|---|---|
| | | Maximum Degree of Rickets Subsequent to Initial Examination | | | | Actively Advancing Rickets with No Evidence of Healing at End of Period of Observation |
| Year of Observation | Total No. of Infants | No Rickets | Extremely Slight Rickets | Mild Rickets | Moderate and Marked Rickets | |
| 1933-34 | 65 | 55 | 22 | 15 | 8 | 18 |
| 1934-35 | 104 | 47 | 10 | 27 | 16 | 16 |
| 1935-36 | 75 | 51 | 16 | 20 | 13 | 31 |
| Total, 1933-36 | 244 | 50 | 15 | 22 | 13 | 21 |

rickets was determined solely on the basis of roentgenograms of the wrists which were taken at the beginning at the middle and at the end of the periods of observation.

Dr. Martha Eliot, assistant chief of the Children's Bureau, United States Department of Labor, Washington, D. C., interpreted all the roentgenograms. The plates were read not only to ascertain the degree of the rachitic process but also to learn whether the process was actively advancing or if there were evidences of healing. Table 2 shows the maximum degrees of rickets which developed during the periods of observation in infants of all the groups studied, together with the percentage of infants in each of the groups who at the end of the periods of observation showed evidence of an actively advancing rachitic process.

In table 3 is given the maximum degree of rickets observed at any time subsequent to the initial examination in infants who received no vitamin D preparation. In this table is also given the percentage of infants showing evidence of an actively advancing rachitic process at the final examination.

2. Drake, T. G. H.; Tisdall, F. F., and Brown, A.: Canad. M. A. J. **31**: 368, 1934 (table XII).

COMMENT

It is to be noted that of the 244 infants receiving no vitamin D, 13 per cent had rickets of a moderate or marked degree during the periods of observation. Also at the end of the five month period, 21 per cent of the 244 infants showed an actively advancing rachitic process without evidence of healing.

During the first year of the observations, in view of the facts that the customary daily dose of cod liver oil is 3 teaspoonfuls (1,000 U. S. P. units) and that the usual dose of viosterol is 10 drops (2,000 U. S. P. units) daily, it was decided to observe the effect of the daily administration of one, two and three teaspoonfuls of cod liver oil and one and one-quarter, two and one-half, five and ten drops of viosterol. It was thought that the lower amounts of each of the products would probably be too small to be effective in the prevention of rickets and thus would afford a means of making a fairly accurate comparison of their antirachitic effects. Surprisingly, however, it became evident that, as shown in table 2, one and one-quarter drops of viosterol (270 U. S. P. units) was just as effective as 10 drops of viosterol (2,160 U. S. P. units) in the prevention of rickets. Also no evidence was found that 3 teaspoonfuls of cod liver oil (1,000 U. S. P. units) was any more effective than 1 teaspoonful (330 U. S. P. units); in fact, the results obtained with 1 teaspoonful were better than those obtained with either 2 or 3 teaspoonfuls, which can be explained only by taking account of the difficulty in administration of the larger amounts. Every possible care was taken to insure the regular administration of the amounts prescribed, and in any instance in which evidence of maladministration was found the case was promptly excluded from this series. It also is to be noted that the daily administration of 500 U. S. P. units of vitamin D in the form of irradiated yeast was slightly more effective in the prevention of rickets than were the varying amounts of viosterol used. This is no doubt accounted for by the fact that, for ease of administration, the irradiated yeast was mixed with cereal and given only to those children who were old enough to be receiving cereal; hence the average age of the infants in this group was slightly greater than that of the babies in the other groups.

During the past winter the amount of cod liver oil administered daily was reduced to slightly less than ½ teaspoonful (150 U. S. P. units). It was seen that the antirachitic effect of this very small amount of cod liver oil was as great as that secured with amounts varying from 1 to 3 teaspoonfuls (table 2). For purposes of comparison, a daily dose of 150 U. S. P. units of vitamin D in the form of a mixture of fish liver oils of high potency (percomorph liver oil) was administered to the infants in another group, and the same number of U. S. P.

units in the form of irradiated cholesterol was given daily to the babies in still another group.[3] In no instance did moderate or marked rickets develop. The numbers of infants with mild rickets and with extremely slight rickets were approximately the same in the different groups. It is evident, therefore, that rat unit for rat unit equally good results were obtained with cod liver oil, percomorph liver oil and irradiated cholesterol.

Some observers have expressed the belief that irradiated milk is a more effective antirachitic substance for human use than are other forms of vitamin D, rat unit for rat unit. In this series of cases irradiated fresh milk has been administered to babies in one group and irradiated evaporated milk to infants in another group in the amounts in which they required milk. The irradiated milk was the sole source of vitamin D given to these infants, and it furnished from 47 to 196 U. S. P. units daily (table 2). The infants received increasing amounts of vitamin D as, with advancing age, they needed greater amounts of milk. However, the babies in another group received exactly 20 ounces (592 cc.) of irradiated fresh milk daily (95 U. S. P. units) throughout the five month period of observation. It is of interest to note that the antirachitic effect of the daily dose of 95 U. S. P. units of vitamin D in the form of irradiated fresh milk was approximately equal to that obtained when 150 U. S. P. units of vitamin D in the form of other substances was administered. This means that probably the dosages have not yet been reached at which it is possible to make the most accurate comparison of the antirachitic values of the different substances tested. However, I believe there is sufficient evidence to indicate that there is no essential difference in the antirachitic potency of vitamin D in the form of cod liver oil, of mixed fish liver oils of high potency, or irradiated cholesterol and of irradiated milk. Although in this study viosterol was not administered in doses as low in content of vitamin D as were the doses of the other substances used, the results indicate that the antirachitic effectiveness of viosterol in human beings is not appreciably less, rat unit for rat unit, than that of the other forms of vitamin D.

During the past two years my associates and I have been able to observe the curative effect of comparatively small amounts of irradiated cholesterol and of irradiated yeast on patients with rickets. During the winter of 1935 it was observed that in 8 patients the daily administration of 750 U. S. P. units of vitamin D in the form of irradiated cholesterol produced definite healing of rickets of moderate or marked

3. Mead Johnson & Co. furnished the mixture of fish liver oils of high potency (percomorph liver oil), and E. I. Du Pont de Nemours & Co. furnished the irradiated cholesterol.

degree in from two to four weeks. During the winter of 1936 similar results were obtained in 3 consecutive patients who received only 300 U. S. P. units of vitamin D daily in the form of irradiated cholesterol and also in 4 consecutive patients who received 500 U. S. P. units daily in the form of irradiated yeast.

## CONCLUSIONS

No evidence was obtained of any difference in the antirachitic effectiveness in human beings, rat unit for rat unit, of vitamin D administered in the form of cod liver oil, of a mixture of fish liver oils of high potency (percomorph liver oil), of irradiated cholesterol, of irradiated fresh milk or of irradiated evaporated milk.

No evidence was observed of any difference in the antirachitic effectiveness in human beings between the daily administration of 150 U. S. P. units of vitamin D in the form of any of the other substances mentioned and that of 270 U. S. P. units of vitamin D in the form of viosterol. As smaller amounts of viosterol were not administered, it is entirely possible that this substance is as effective in human beings, rat unit for rat unit, as are the others.

The administration of vitamin D in amounts as low as 95 U. S. P. units daily prevented the development of rickets of a moderate or marked degree in every case. No evidence was obtained that this extremely small amount was less effective in preventing rickets, as measured by roentgenograms, than were the larger amounts usually administered.

Rapid healing of rickets of moderate or marked degree resulted from the daily administration of as little as 300 and 500 U. S. P. units of vitamin D. The 300 U. S. P. units of vitamin D was administered in the form of irradiated cholesterol, and the 500 U. S. P. units, in the form of irradiated yeast.

# PROPHYLAXIS OF WHOOPING COUGH

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Whooping cough is an important disease among young children. The dangers from complications warrant any effort to protect young children from becoming the victims of this infection. The difficulty of early diagnosis and the unsatisfactoriness of the measures which have been used in years past to obtain active immunity have stimulated further inquiry into the matter of passive immunization by means of the blood serum of persons who have recovered from the disease. The successful use of convalescent scarlet fever serum suggests that human serum from persons who have recovered from whooping cough may be useful in decreasing the incidence of the disease among the very young.

To measure the value of human blood serum in prophylaxis for young children who have been exposed to whooping cough, a group of control children must be selected who are similar in all respects except that they have not had this serum. To secure comparable groups certain considerations must be adopted.

1. Children of the same age must be used for both the treated and the untreated group. Since the number of children over 6 years of age who were treated was too small to be of significance, no data concerning children over 6 years of age in the control group are included.

2. The period of exposure for the control group must correspond to the period of exposure for treated children. The same proportion of children who have been exposed for one, two, three or four weeks should be incorporated in the control group as in the group of treated children.

3. The ratio of associated children (the children in whom whooping cough first developed, by whom the others were exposed) to exposed children in the treated and in the untreated group should be as nearly alike as possible.

4. Children who have previously had whooping cough should not be included in either the treated or the untreated group.

5. The serum must not be expected to give protection after half of the incubation period has passed. This is an arbitrary statement which may or may not subsequently prove to be true, but in this study it is observed. Assuming that the average incubation period for whooping cough is twelve days, the serum must not be expected to protect those

to whom it is given after the first six days of the incubation period. For convenience in this study, when whooping cough developed within six days from the time the child received the serum this is not counted as a failure for the serum.

6. Again, the serum must not be expected to give protection for longer than three weeks. Hence, when whooping cough developed after three weeks from the time the serum was given this is not recorded as a failure of the serum.

7. For the purpose of this study, a patient is considered a positive source of infection for four weeks.

8. Ten cubic centimeters of pooled blood serum from patients who had recovered from whooping cough was injected subcutaneously into the treated exposed children.

The records used in this study were made during the years 1928 and 1929. The study is limited to children whose records were complete and were believed reliable when they were compiled. In Detroit during 1928, 5,395 cases of whooping cough were reported, in 85 of which the patient died. The following year 4,100 cases were reported, in 90 of which the patient died. The estimated number of children under 10 years of age in the city during this period was 283,000.

TABLE 1.—*Data on Treated Exposed Children*

| Age, Yr. | No. of Children | No. Without Whooping Cough | No. with Whooping Cough | Incidence of Whooping Cough, Percentage |
|---|---|---|---|---|
| 0-2 | 24 | 14 | 10 | 41.7 |
| 2 | 25 | 15 | 10 | 40.0 |
| 3 | 17 | 13 | 4 | 23.5 |
| 4 | 21 | 18 | 3 | 14.3 |
| 5 | 17 | 12 | 5 | 29.4 |
| 6 | 11 | 6 | 5 | 45.5 |
| Total | 115 | 78 | 37 | 32.2 |

From table 1 it is apparent that 115 children of ages from 1 to 6 years were treated with 10 cc. of blood serum from persons who had recovered from whooping cough. Whooping cough developed in 37, or 32.2 per cent.

A study was made of the period between the date the blood serum was given to the exposed children and the time the disease developed. These data are presented in table 2.

From table 2 it appears that whooping cough developed in 8 children on the first day after the serum was given. Manifestly, the record in these cases should not discredit the value of the serum. According to the premise stated at the beginning, the fact that the disease developed

during the first six days after administration of the serum should not be counted against the serum. Twenty-one patients should therefore be excluded. Table 2 shows that in only 16 of the 37 cases failure should be charged against the serum. Table 2 also shows that in only 1 of the 16 patients whom the serum did not protect did the disease develop after fourteen days from the time the serum was given; in this patient it developed on the eighteenth day. The serum was given to that child on the fourth day after exposure.

Table 3 was prepared as a modification of table 2 to show the number by age groups in whom whooping cough developed and the number of days of exposure to whooping cough. The table also shows the percentage by age groups in whom whooping cough developed.

Table 3 shows that a total of 94 treated exposed children are left for study, in 16 of whom, or 17 per cent, whooping cough developed

TABLE 2.—*Length of the Interval Between the Administration of the Serum and the Onset of the Disease for Treated Exposed Children in Whom Whooping Cough Developed*

| Age, Yr. | No. of Children | Days | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 |
| 1 | 10 | 2 | 1 | 1 | 1 | .. | .. | 1 | 2 | .. | .. | 1 | .. | .. | 1 | .. | .. | .. | .. |
| 2 | 10 | 4 | 1 | 1 | 1 | .. | 2 | .. | .. | .. | .. | .. | .. | .. | 1 | .. | .. | .. | .. |
| 3 | 4 | 1 | .. | .. | .. | .. | 1 | .. | 1 | .. | .. | .. | .. | .. | 1 | .. | .. | .. | .. |
| 4 | 3 | 1 | .. | .. | .. | .. | .. | 1 | .. | .. | .. | .. | .. | .. | 1 | .. | .. | .. | .. |
| 5 | 5 | .. | .. | .. | .. | 1 | .. | .. | 1 | .. | 1 | .. | .. | .. | 1 | .. | .. | .. | 1 |
| 6 | 5 | .. | 1 | .. | .. | 2 | .. | .. | 2 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Total | 37 | 8 | 3 | 2 | 2 | 3 | 3 | 2 | 6 | .. | 1 | 1 | .. | .. | 5 | .. | .. | .. | 1 |

and in 78 of whom it did not develop. The question arises, Of the 94 children treated, in how many would whooping cough have developed had they not received convalescent serum? The answer to that question is found in a study of our control group.

For control children, 183 children of ages from 1 to 6 were used who were exposed to whooping cough but who were not given blood serum from persons who had recovered from this disease. Whooping cough developed in 121, or 66 per cent, of these 183 children.

Before accepting these exposed children as suitable control children, it is necessary to examine the period in which each was exposed to whooping cough before it developed in him. Table 5 has been prepared for that purpose.

From table 5 it will be noted that the disease developed in 8 untreated exposed children two days after the first exposure. Of course, these children are unsuitable for comparison, since whooping cough never develops within two days. They became infected at the same time that the associated children became infected. In fact, none of the untreated

TABLE 3.—*Data on Treated Exposed Children*

| Age, Yr. | No. of Children | No. without Whooping Cough | No. with Whooping Cough | Incidence of Whooping Cough, Percentage | Days Between First Exposure and Onset of Disease | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 |
| 1 | 19 | 14 | 5 | 26 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | 3 | .. | .. | .. | .. | .. | .. | .. | .. | 2 | .. | .. | .. | .. | .. | .. | .. | .. |
| 2 | 16 | 15 | 1 | 6 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | 1 |
| 3 | 15 | 13 | 2 | 13 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | 1 | .. | .. | .. | .. | .. | .. | .. | .. | 1 | .. | .. | .. | .. | .. | .. | .. | .. |
| 4 | 20 | 18 | 2 | 10 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | 1 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | 1 |
| 5 | 16 | 12 | 4 | 25 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | 1 | .. | .. | .. | 1 | .. | .. | .. | .. | 1 | 1 | .. | .. | .. | .. | .. | .. | .. |
| 6 | 8 | 6 | 2 | 25 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | 1 | .. | .. | .. | .. | .. | .. | .. | 1 | .. | .. | .. | .. |
| Total | 94 | 78 | 16 | 17 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | 5 | .. | .. | .. | 2 | 1 | .. | .. | .. | 4 | 1 | .. | .. | 1 | .. | .. | .. | 2 |

exposed children in whom the disease developed during the first six days of recorded exposure should be accepted for comparison with the treated exposed children. Furthermore, those in whom the disease developed later than twenty-nine days after the first exposure should not be accepted for comparison with the treated exposed children because those in the treated group in whom whooping cough developed later than twenty-nine days after exposure were not included (table 3). One must therefore remove 29 untreated exposed children from those considered in table 5 to secure a group of control children who are comparable with the treated exposed children. It may be urged that they were exposed at some time and that if the point of exposure could be determined they might be entered, with the onset of the disease placed further along in the table. The same argument may be used about the treated exposed children. In both instances it is not possible to secure

TABLE 4.—*Untreated Exposed Children (Control Children)*

| Age, Yr. | No. of Children | No. without Whooping Cough | No. with Whooping Cough | Incidence of Whooping Cough, Percentage |
|---|---|---|---|---|
| 1 | 44 | 12 | 32 | 72.4 |
| 2 | 34 | 6 | 28 | 82.2 |
| 3 | 25 | 5 | 20 | 80.0 |
| 4 | 30 | 10 | 20 | 66.8 |
| 5 | 30 | 15 | 15 | 50.0 |
| 6 | 20 | 14 | 6 | 30.0 |
| Total | 183 | 62 | 121 | 66.0 |

this information, so it seems wiser to exclude from both the group of treated and that of untreated exposed children all the children in whom the disease developed within the first six days of recorded exposure or after twenty-nine days.

It is of interest to note the relation of associated children to exposed children. The proportion of associated children to treated exposed children is 67 to 94, or 1 to 1.4, and of associated children to untreated exposed children, 84 to 154, or 1 to 1.8. The relative amount of "seeding" by patients with whooping cough is therefore reasonably uniform.

It is of interest further to note the age of the associated children for both the treated and the untreated group. The average age of the children associated with the treated exposed children in whom whooping cough developed was 4.4 years and that of the children associated with treated exposed children in whom the disease did not develop was 5.6 years. For the untreated group the average age of the children associated with exposed children in whom the disease developed was 4.4 years, while that of the children associated with exposed children in whom whooping cough did not develop was 3.8 years.

TABLE 5.—*Data on Untreated Exposed Children (Control Children) in Whom Whooping Cough Developed*

| Age, Yr. | No. of Children | Days Between First Exposure and Onset of Disease | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 | 33 |
| 1 | 32 | .. | 1 | .. | 2 | 3 | 1 | 3 | 3 | .. | 1 | 4 | 3 | .. | 2 | 2 | .. | 1 | 1 | 1 | .. | .. | .. | .. | .. | .. | .. | .. | 2 | 1 | .. | 1 | .. | .. |
| 2 | 28 | .. | 2 | .. | 1 | 1 | 1 | 4 | 2 | 1 | 4 | 1 | 1 | .. | .. | 1 | .. | .. | 1 | .. | 3 | 2 | .. | 1 | .. | .. | .. | .. | .. | 1 | .. | .. | .. | 1 |
| 3 | 20 | .. | 2 | .. | .. | 2 | .. | 4 | .. | .. | 1 | .. | 1 | .. | 2 | 3 | .. | .. | 2 | 3 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| 4 | 20 | .. | 1 | .. | 2 | 1 | .. | 4 | 2 | 1 | 2 | 2 | .. | 1 | .. | .. | .. | .. | .. | .. | .. | .. | 1 | 1 | .. | .. | .. | .. | 1 | .. | 1 | .. | .. | .. |
| 5 | 15 | .. | 2 | 1 | 2 | .. | .. | 4 | 1 | 1 | .. | .. | 1 | .. | .. | .. | .. | 1 | .. | 1 | 1 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| 6 | 6 | .. | .. | .. | 1 | .. | .. | .. | .. | 1 | .. | .. | 1 | .. | 1 | .. | 1 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | 1 | .. | .. | .. | .. | .. | .. |
| Total | 121 | .. | 8 | 1 | 8 | 7 | 2 | 19 | 8 | 4 | 8 | 7 | 7 | 1 | 5 | 6 | 1 | 2 | 4 | 5 | 4 | 2 | 1 | 2 | .. | .. | .. | 1 | 3 | 2 | 1 | 1 | .. | 1 |

TABLE 6.—*Data on Selected Untreated Exposed Children (Control Children)*

| Age, Yr. | No. of Children | No. without Whooping Cough | No. with Whooping Cough | Incidence of Whooping Cough, Percentage | Days Between First Exposure and Onset of Disease | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 |
| 1 | 36 | 12 | 24 | 66.6 | .. | .. | .. | .. | .. | .. | .. | 3 | 3 | .. | 1 | 4 | 3 | .. | 2 | 2 | .. | 1 | 1 | 1 | .. | .. | .. | .. | .. | .. | .. | .. | 2 | 1 |
| 2 | 28 | 6 | 22 | 79.0 | .. | .. | .. | .. | .. | .. | .. | 4 | 2 | 1 | 4 | 1 | 1 | .. | .. | 1 | .. | .. | 1 | .. | 3 | 2 | .. | 1 | .. | .. | .. | .. | .. | 1 |
| 3 | 21 | 5 | 16 | 76.0 | .. | .. | .. | .. | .. | .. | .. | 4 | .. | .. | 1 | .. | 1 | .. | 2 | 3 | .. | .. | 2 | 3 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| 4 | 25 | 10 | 15 | 60.0 | .. | .. | .. | .. | .. | .. | .. | 4 | 2 | 1 | 2 | 2 | .. | 1 | .. | .. | .. | .. | .. | .. | .. | .. | 1 | 1 | .. | .. | .. | .. | 1 | .. |
| 5 | 25 | 15 | 10 | 40.0 | .. | .. | .. | .. | .. | .. | .. | 4 | 1 | 1 | .. | .. | 1 | .. | .. | .. | .. | 1 | .. | 1 | 1 | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| 6 | 19 | 14 | 5 | 26.3 | .. | .. | .. | .. | .. | .. | .. | .. | .. | 1 | .. | .. | 1 | .. | 1 | .. | 1 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | 1 | .. | .. |
| Total | 154 | 62 | 92 | 60.0 | .. | .. | .. | .. | .. | .. | .. | 19 | 8 | 4 | 8 | 7 | 7 | 1 | 5 | 6 | 1 | 2 | 4 | 5 | 4 | 2 | 1 | 2 | .. | .. | .. | 1 | 3 | 2 |

A study of the period of exposure to whooping cough of the children in the treated and in the untreated group was made. It was found that the periods of exposure in both groups were well distributed, so that they could be considered comparable.

One should bear in mind when selecting control children for comparison that the period to compare is that in which susceptibility exists. For example, if in a family of 3 children 1 has whooping cough, the disease develops in a second after the usual incubation period, perhaps twelve days, while in the third it does not develop at all, the period of exposure of the second and the third child would be the same, but the period of presumable susceptibility of the second child would be less than that of the third. For the purpose of comparison with that of other children, the period of exposure for the second child would be the period from the first exposure to the date of the onset of whooping

TABLE 7.—*Summary of Data*

| Age, Yr. | Treated Exposed Children | | | Percentage in Whom Whooping Cough Should Develop | Calculated Number in Whom Whooping Cough Should Develop |
|---|---|---|---|---|---|
| | No. of Children | No. without Whooping Cough | No. with Whooping Cough | | |
| 1 | 19 | 14 | 5 | 66.6 | 13 |
| 2 | 16 | 15 | 1 | 79.0 | 13 |
| 3 | 15 | 13 | 2 | 76.0 | 11 |
| 4 | 20 | 18 | 2 | 60.0 | 12 |
| 5 | 16 | 12 | 4 | 40.0 | 6 |
| 6 | 8 | 6 | 2 | 26.0 | 2 |
| Total | 94 | 78 | 16 | 60.0 | 57 |

cough, twelve days, while the period of exposure for the third child should be recorded as the period from the first exposure until the sign on the home was removed, or the period of communicability in 2 cases, i. e., fifty-six days (see premise 7). If the home was placarded forty days, the third child would be exposed for sixteen days to 2 infected children.

Table 6 is presented to show data on the selected untreated exposed children who are used as controls.

There were 154 exposed children, in 92, or 60 per cent, of whom whooping cough developed. In table 6 will be noted the percentage of each age group in whom the disease developed—in 66.6 per cent of the children aged 1 year, in 79 per cent of the children aged 2 years, and so on. An application of these percentages to the treated exposed children apparently indicates the number of those in whom whooping cough would have developed if the serum had not been given.

Applying the aforementioned percentages to the treated exposed children by the age groups mentioned in table 3, one has a calculated

number of exposed children in whom whooping cough would have developed if the serum had not been given. The total of this number is noted in table 7 to be 57, but actually whooping cough developed in only 16, so that 41 (57 minus 16), or 72 per cent, were apparently protected from whooping cough by the use of the convalescent serum.

### COMMENT

The tables indicate that when comparable groups of treated and untreated exposed children are compared, about 72 per cent of those treated with 10 cc. of pooled convalescent serum will be protected from this disease. The incubation period is so long that while 1 of 2 children in a given family, receiving the serum prophylactically at a fortuitous moment, will be protected, another, receiving the serum in the latter part of the incubation period, will contract whooping cough, apparently having received no protection. This serum will therefore probably never be as spectacular in its effects as similar convalescent serum is for scarlet fever, for which a short incubation period prevails.

For the physician who understands the precise use of convalescent whooping cough serum and has an opportunity to use it skilfully, a considerable reward will be obtained. The use of a larger dose would presumably enhance the results. If the physician can give from 10 to 15 cc. of pooled blood serum from persons who have recovered from whooping cough to children who have been exposed not more than six or seven days, about three quarters of the children who otherwise would acquire the disease will be protected. The most favorable results are obtained with children in the first three years of life.

# HUMAN MILK: ITS LYSOZYME CONTENT AND BACTERIAL COUNT

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There is a constant and striking difference in the bacteriologic findings in the stool of the breast-fed and the artificially fed infant. In the stool of the former gram-positive bacilli predominate, while in that of the latter [1] gram-negative, morphologically dissimilar organisms are in excess.

To ascertain the significance of this variation and its importance in the problem of infant feeding were the objectives of this investigation. The introductory phase—the study of lysozyme in human milk and its relation to the bacterial flora of the milk—was begun in 1934 and is the subject of this paper.

In 1931 Rosenthal and Lieberman [2] reported the influence of lysozyme in the development of the intestinal flora of infants. They found a lytic principle in the stools of nurslings which they tested against cultures of gram-positive sarcinas. It was inactivated by heating at 65 C. for one and a half hours or by boiling for three minutes. Rosenthal and Lieberman identified this substance as lysozyme. It was absent from the stools of artificially fed infants and from the meconium of nurslings for the first two days, but it was constantly present after the fourth day in the stools of breast-fed babies. Lysozyme was present in all samples of colostrum and breast milk but absent from cows' milk and from the modified milk commonly used in feeding infants. It inhibited growth of Bacillus coli at 37 C., and the organism was lysed at 56 C. Bacillus bifidus was not disintegrated by lysozyme. Rosenthal and Lieberman concluded that lysozyme tends to stabilize the gram-positive intestinal flora of nurslings.

Fleming [3] in 1922 called attention to a substance present in tissues and secretions with "properties akin to ferments." He applied the

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1. Morris, G. B.; Porter, R. L., and Mayer, K. F.: J. Infect. Dis. **25**:349. 1919. Freudenberg, E.: Physiologie und Pathologie der Verdauung im Säuglingsalter, Berlin, Julius Springer, 1929.

2. Rosenthal, L., and Lieberman, H.: J. Infect. Dis. **48**:226, 1931.

3. Fleming, A.: Proc. Roy. Soc., London, s. B **93**:306, 1922.

term "lysozyme" to this substance, which he found in all human tissues and secretions except in normal urine, cerebrospinal fluid and sweat. It was also present in animal tissues, egg white and turnips.

Its characteristic quality was the dissolution of live bacteria in culture. It lysed 75 per cent of one hundred and four strains of bacteria obtained from the air, seven of eight pathogenic organisms, twelve of eighteen strains of intestinal streptococci, B. coli and typhoid bacilli.

Fleming observed that lysozyme was soluble in water and in physiologic solution of sodium chloride but insoluble in chloroform, ether and toluene. Lysozyme retained its potency at room temperature, remained active when dried in egg white and was precipitated from albuminous fluids by protein precipitants. Its activity was destroyed by a 5 per cent solution of sodium chloride. The lytic effect was most pronounced at a $p_H$ of 7. The thermostability of lysozyme differed somewhat, depending on the source of the substance, only seven and a half minutes at 75 C. being necessary to destroy its action in saliva, while it took one hour of boiling to destroy its action in tears. Its optimum activation occurred at 60 C. It did not pass through a collodion membrane and was adsorbed by a porcelain filter, cotton wool, filter paper and charcoal.

In a later observation, Fleming and Allison [4] stated that with Micrococcus lysodeikticus as an indicator suspensions were cleared with lysozyme in a few seconds. Lysis of suspensions of live and dead bacteria occurred with equal rapidity. Of all the secretions, tears had the highest content of lysozyme, while cartilage contained more than the other tissues. When micro-organisms were inoculated into lysozyme-containing material, there was at first no sign of growth. Later a few scattered colonies appeared, which then were resistant not only to the lytic action of the medium on which they grew but to the lytic action of all other tissues. Fleming and Allison stated that the action of lysozyme on bacterial culture releases a substance lytic to identical strains. It differs from bacteriophage in that the phage acts only on live cultures. The optimum temperature for bacteriophage activity is within extremely narrow limits; and, according to d'Herelle and others, its activity may be transmitted to other cultures. This is not true of lysozyme. Its activity decreases with dilution. Furthermore, the small, round, clear area in the colonies—the "plaques" characteristic of bacteriophage—are not found on solid mediums to which lysozyme has been added.

In 1927 Wolff [5] confirmed Fleming's work. He isolated lysozyme from egg white in a pure state and inoculated it into rabbits and guinea-pigs. No local reaction or anaphylactic shock developed. After subcutaneous or intravenous injection, the presence of lysozyme was

4. Fleming, A., and Allison, V. D.: Brit. J. Exper. Path. **3**:252, 1922.

5. Wolff, L. K.: Ztschr. f. Immunitätsforsch. u. exper. Therap. **54**:188, 1927.

demonstrated in the blood serum and in the urine. Immediately after the injection, there was leukopenia, with a decrease in the number of polymorphonuclear leukocytes, followed by leukocytosis. Wolff reported that lysozyme had bacteriolytic action on Bacillus anthracis, as well as on several strains of staphylococci.

Schlaeppi [6] in 1928 reported some interesting observations on the bactericidal properties of human milk. He made bacterial counts on milk obtained from cleaned and uncleaned breasts at regular intervals after expression of the milk. He noted that there was an inhibition in the growth of organisms in the milk a few hours after it was obtained from the breast. This lasted for about sixty hours at a temperature of from 17 to 23 C., was greater at from 10 to 13 C. and was very little at from 30 to 37 C. The inhibitive power was more pronounced in milk from cleaned breasts. Schlaeppi observed also that raw milk inhibited the growth of B. coli. When milk was passed through a silica filter, he found that the bactericidal principle was contained in the filtrate and remained active as long as eight days at a temperature of from 18 to 20 C. An individual variation in the bactericidal action of the milk was observed. The action of the bacteria-free filtrate of any mother's milk was more intense against staphylococci cultivated from her own secretion than against those from an abscess in the same woman or from the milk of other nursing mothers. The filtrate was active for months. Schlaeppi concluded that the microflora of the secreting breast were attenuated by the action of the bacteriolytic principle and thus rendered harmless.

In the same year Schlaeppi [7] studied the bacterial content of breast milk. He noted that the bacterial count differed in the milk from individual women. In milk from uncleaned breasts, he observed Staphylococcus albus constantly and Staphylococcus aureus frequently. Milk obtained under aseptic precautions contained fewer bacteria, and of these a greater proportion were Staph. albus. First samples showed more bacteria than later ones.

In 1929 Fleming [8] reported that when large quantities of lysozyme-containing material passed through a Berkefeld filter the enzyme was initially adsorbed but that in the latter portion of the filtrate it came through full strength. Fleming demonstrated that increased resistance to lysozyme could be induced in an organism by subculturing in increasing concentrations of a lysozyme-containing medium. He also observed that bacteria when dissolved by lysozyme do not neutralize the lytic

6. Schlaeppi, F.: Schweiz. Ztschr. f. Gezundheitspflege **8**:373, 1928.

7. Schlaeppi, F.: Arch. f. Protistenk. **63**:105, 1928.

8. Fleming, A.: Lancet **1**:217, 1929.

agent. The lysozyme content was not increased by vaccines. Fleming expressed the opinion that this was proof of its relation to natural rather than to acquired immunity.

In 1930 Florey [9] examined tissues from a number of dead animals and three human bodies in order to determine the relative amounts of lysozyme present. He found that the tissues of each species varied in lysozyme content.

Corper [10] in 1932 reported that lysozyme had no bacteriolytic effect on Mycobacterium tuberculosis.

Bradford and Roberts [11] in 1936 reported a study on the lysozyme content of blood. They noted that the leukocytes were more active than plasma, serum or whole blood when M. lysodeikticus was used as an indicator. The lytic power of the leukocytes was increased in certain acute infections and in treatment by artificial fever and was decreased after the crisis in pneumonia. The lysozyme content of the leukocytes increased or decreased in direct relationship to the percentage of polymorphonuclear leukocytes.

## PROCEDURE

The breast milk for this study was obtained from the collecting station established at the Cook County Hospital in 1934 to care for the needs of premature infants.

The mothers whose milk was used were selected after physical examination and a careful review of their histories.[12] All of them were tested serologically for syphilis and examined physically for tuberculosis. Material from their throats was cultured for hemolytic streptococci, and their milk was plated for hemolytic organisms. In addition, their infants were given routine monthly examinations, as a welfare measure. It was found that the Negro mothers secreted a greater amount of milk, were more cooperative and were more reliable in attendance than were the white women. These data relate, therefore, to the milk secreted by Negro mothers, in all but one instance. They were delivered in the obstetric wards of the Cook County Hospital.

A nurse supervised the cleansing of breasts and hands and the sterilization of gowns and apparatus. The milk was expressed manually or with the aid of a hand-operated or an electric breast pump. All aseptic precautions were taken in its collection. It was immediately cooled and sent to the milk laboratory. Here it was pooled, part of it refrigerated and dispensed raw and the remainder boiled before dispensing. Milk obtained in excess of that needed for the day was preserved by placing it in sterile quart mason jars and boiling it in a water bath. The jars of milk were sealed, refrigerated and reboiled in like manner on the two succeeding days. Such milk has been kept for months and dispensed as necessity forces its use.

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9. Florey, H.: Brit. J. Exper. Path. **11**:251, 1930.

10. Corper, H. J.: Am. Rev. Tuberc. **25**:59, 1932.

11. Bradford, W. L., and Roberts, J. B.: J. Pediat. **8**:24, 1936.

12. The assembling of the lactating women was accomplished by Miss Winnie Cox, R.N., of the Cook County School of Nursing.

The lytic value[13] of the specimens of milk was established by the effect of various dilutions of individual samples on standardized cultures of Sarcina lutea from the American Type Culture Collection.

Milk was centrifugated for five minutes, and the supernatant fat was removed. An equal amount of ether was added to this fat-free milk, and the tube containing the mixture was shaken vigorously. The solution was then placed in a water bath, and the ether was evaporated at a temperature not exceeding 55 C.

Two solutions of standardized sarcinas were used. The first, A, consisted of the washing of a twenty-four hour nutrient agar slant with 3 cc. of physiologic solution of sodium chloride. This produced a very cloudy suspension. The second, B, was prepared by washing a similar slant with 15 cc. of physiologic solution of sodium chloride. These suspensions were used as shown in table 1.

The measured quantities of solutions were placed in tubes, and the tubes were corked, agitated and incubated at 55 C. for twenty-four hours. Smears were made from each tube and were stained by the Gram method and read for lysis. Readings of macroscopic turbidity against standardized solutions proved less satisfactory, on account of the translucence of the milk. The scale of lysis in the solution

TABLE 1.—*Arrangement of Tubes for the Determination of Lysis*

| Tube No. | Cc. of Ether-Treated Milk | Cc. of Physiologic Solution of Sodium Chloride | Cc. of Suspension of Sarcinas | Dilution of Milk |
|---|---|---|---|---|
| 1 | 2.0 | 0.0 | 0.3 (A) | 1:1.5 |
| 2 | 0.2 | 0.8 | 1 (B) | 1:10 |
| 3 | 0.02 | 0.98 | 1 (B) | 1:100 |
| 4 | 0.002 | 0.998 | 1 (B) | 1:1,000 |
| 5 | 0.0002 | 0.9998 | 1 (B) | 1:10,000 |

from each tube was from 0 to 4; 0 showed no evidence of lysis, whereas a slide recorded as 4 presented the picture of complete bacterial dissolution, a stained smudge. The dissolution was so complete that no tinctorial evidence of organisms remained. Between these two extremes, various degrees of lysis were recorded as 1, 2 and 3. In these intermediate stages, the organisms became increasingly swollen and took the stain poorly.

We have coined the term "lytic index" for the sum obtained by adding the integers representing the degree of lysis in each of the five tubes diluted, as shown in table 1. Smears from each specimen as seen on the gram-stained slide were so recorded in the tables. This figure provides a quantitative standard for comparison of the lysozyme contents of the various specimens.

## OBSERVATIONS

To determine the effect of heat, ten individual samples of human milk were brought to a boil, as for ward distribution, and then tested for lytic action. It was found that boiling always markedly reduced and in one instance entirely eliminated such action (table 2).

13. The technic was developed by Dr. Paul Prickett, of the laboratories of Mead Johnson & Co. He described it in a personal communication.

Four specimens of the milk fractionally sterilized for prolonged preservation, as previously described, were similarly examined for lytic action. Three showed a negative result, and one gave a lytic index of 1. Repeated boiling inactivated the lysozyme in human milk.

Five specimens of raw certified cows' milk were examined and found to have little or questionable lytic action on sarcinas. This confirmed the work of Rosenthal and Lieberman.[2]

These facts having been established, it was decided that raw human milk should be fed premature infants. The possibility that control of the gastro-intestinal flora might eliminate diarrhea and allow a greater caloric intake by premature infants made the problem clinically interesting. This possibility was based on the fact that the stool of the breast-fed infant has a predominantly gram-positive, aciduric, non-

TABLE 2.—*Thermolability of the Lytic Principle in Human Milk*

| Wet Nurse | Lytic Index | |
|---|---|---|
| | Before Boiling | After Boiling |
| P. | 15 | 6 |
| C. | 9 | 5 |
| S. | 14 | 2 |
| H. | 14 | 4 |
| S. | 13 | 3 |
| Co. | 13 | 6 |
| H. | 11 | 0 |
| A. | 11 | 3 |
| H. | 11 | 3 |
| C. | 10 | 4 |
| Average | 12.1 | 3.6 |

pathogenic flora, in contrast to that of the artificially fed infant. Before instituting the procedure, the bacteriologic and lytic activity of a large series of samples of human milk was investigated.

Bacterial counts were made on plate cultures of forty samples. The samples were obtained by pooling milk collected at the same hour from several wetnurses, who appeared at the station for collection of milk at 8 a. m. and 2 p. m. daily. The pooled samples were held in the refrigerator at from 9 to 12 C. for four days and some of them plated each day. As it was thought that raw human milk would rarely be used longer than twenty-four hours after expression, the majority of the samples were examined at the end of that period (table 3).

The forty counts gave a general idea of the number of bacteria in raw milk collected as previously described. The counts were made on different specimens after varying periods of refrigeration and were not serial. The rate of increase of bacteria in raw breast milk under the conditions of this observation was slow.

The cultures were made according to the procedure outlined by the American Public Health Association.[14] Milk was diluted 1 : 10 and 1 : 100 in sterile distilled water, and poured plate cultures were made on standard nutrient agar, 1 cc. of the dilution being used.

In examination of cows' milk, the American Public Health Association has recommended that only those plates be counted on which a colony count of between 30 and 300 per cubic centimeter occurred. This method appeared to us as not applicable in the examination of fresh human milk. This conclusion is based on the fact that of eighty-five specimens noted in table 5, seven gave a count of zero, and twenty-six additional plates had less than 30 colonies (table 4). Of the twenty-six with counts of less than 30, bacterial growth occurred in ten for which the 1 : 10 dilution was used. No growth occurred in

TABLE 3.—*Highest, Lowest and Average Bacterial Counts for Pooled Raw Refrigerated Human Milk, from Twelve to Ninety-Six Hours After Expression*

| No. of Samples Examined | Hours After Expression | Bacterial Counts | | |
|---|---|---|---|---|
| | | Lowest | Highest | Average |
| 2 | 12 | 2,000 | 3,000 | 2,500 |
| 21 | 24 | 0 | 7,000 | 1,864 |
| 10 | 48 | 200 | 23,000 | 3,275 |
| 6 | 72 | 0 | 6,800 | 2,726 |
| 1 | 96 | 2,000 | 2,000 | 2,000 |

those for which the 1 : 100 dilution of these same specimens was used. In two of the remaining sixteen plates, 1 and 2 colonies, respectively, occurred in the 1 : 100 dilution, while the 1 : 10 dilutions were free from colonies. The apparent discrepancy between the counts for these two dilutions may be explained by contamination in transferring mediums. Such results do not, however, interfere with the conclusion that aseptically collected breast milk has an exceedingly low bacterial colony count. Counts lower than those recommended in the commercial examination of cows' milk were therefore used and in our opinion are acceptable.

To recapitulate, thirty-three of eighty-five plates showed fewer colonies than recommended for counting by the American Public Health Association. In view of the fact that the same technician (H. K.), using the same technic, obtained a high count in fifty-two specimens collected in the same manner, we assume that these figures are correct. Elimination of the low counts from our tables would have resulted in averages much higher than we believe existed.

14. Standard Methods of Milk Analysis, ed. 6, New York, American Public Health Association, 1934.

The "average" bacterial counts recorded in the tables, were obtained as follows: When the count for either the 1:10 or the 1:100 dilution was zero and the second plate showed colonies, the count was taken from the latter plate. Usually the counts recorded were averages for the two dilutions. In all tables, the figures under the heading "Bacterial Counts" represent the number of colonies multiplied by the milk dilution factor. Colony counts were recorded at the end of a forty-eight hour period of incubation. A number of plates were held

TABLE 4.—*Analysis of Bacterial Counts of Less than 300 per Cubic Centimeter for Raw Human Milk*

| Wetnurse | Number of Colonies | |
|---|---|---|
| | 1:10 Dilution | 1:100 Dilution |
| 5-M | 0 | 0 |
| 26-C | 0 | 0 |
| 26-C | 0 | 0 |
| 26-C | 0 | 0 |
| 21-H | 0 | 0 |
| 21-H 6 | 0 | 0 |
| 6-C | 0 | 0 |
| 5-M | 1 | 0 |
| 21-H | 1 | 0 |
| 6-C | 1 | 0 |
| 14-S. C | 2 | 0 |
| 14-S. C | 2 | 0 |
| 5-M | 3 | 0 |
| 21-H | 3 | 0 |
| 14-S. C | 3 | 0 |
| 26-C | 4 | 0 |
| 27-McG | 5 | 0 |
| 14-S. C | 1 | 1 |
| 5-M | 2 | 1 |
| 27-McG | 4 | 1 |
| 6-C | 16 | 1 |
| 6-C | 0 | 1 |
| 18-O | 12 | 1 |
| 11-P | 3 | 2 |
| 20-W | 16 | 1 |
| 26-C | 16 | 1 |
| 12-P | 18 | 1 |
| 27-McG | 3 | 3 |
| 8-R | 0 | 2 |
| 12-P | 24 | 2 |
| 28-J | 8 | 4 |
| 21-H | 4 | 5 |
| 29-A | 28 | 1 |

in the incubator, and readings were made at the end of seventy-two and of ninety-six hours to assure the appearance of any slowly growing micro-organism. In a few instances, additional colonies appeared after seventy-two hours, but the number was too small to make the difference worth recording.

The use of dextrose agar as a medium for the preparation of plate cultures of human milk for which bacterial counts are to be made was recommended by Schlaeppi.[7] However, we found that the count in most instances was higher when the nutrient agar recommended by the American Public Health Association was used. This was explained by

TABLE 5.—*Bacterial Counts and Lysozyme Content of Eighty-Five Samples of Human Milk, Freshly Obtained and Manually Expressed*

| Wetnurse | Bacterial Counts | Lysis at Various Dilutions | | | | | Lytic Index |
|---|---|---|---|---|---|---|---|
| | | 1:1.1 | 1:10 | 1:100 | 1:1,000 | 1:10,000 | |
| 5-M | 0 | 4 | 4 | 4 | 3 | 2 | 17 |
| 26-C | 0 | 4 | 4 | 3 | 2 | 1 | 14 |
| 26-C | 0 | 4 | 4 | 3 | 2 | 1 | 14 |
| 26-C | 0 | 4 | 4 | 3 | 2 | 1 | 14 |
| 21-H | 0 | 4 | 4 | 3 | 2 | 1 | 14 |
| 21-H | 0 | 4 | 4 | 4 | 2 | 1 | 15 |
| 6-C | 0 | 4 | 4 | 4 | 3 | 3 | 18 |
| 5-M | 10 | 4 | 4 | 4 | 4 | 1 | 17 |
| 21-H | 10 | 3 | 3 | 2 | 2 | 1 | 11 |
| 6-C | 10 | 4 | 4 | 4 | 3 | 3 | 18 |
| 14-S. C | 20 | 4 | 4 | 3 | 2 | 2 | 15 |
| 14-S. C | 20 | 4 | 4 | 4 | 3 | 3 | 18 |
| 5-M | 30 | 4 | 4 | 4 | 1 | 1 | 14 |
| 21-H | 30 | 4 | 4 | 3 | 1 | 0 | 12 |
| 14-S. C | 30 | 4 | 4 | 3 | 3 | 3 | 17 |
| 26-C | 40 | 4 | 2 | 1 | 1 | 0 | 8 |
| 27-McG | 50 | 4 | 3 | 2 | 2 | 0 | 11 |
| 14-S. C | 55 | 4 | 4 | 3 | 3 | 3 | 17 |
| 5-M | 60 | 4 | 4 | 4 | 4 | 1 | 17 |
| 27-McG | 70 | 4 | 2 | 2 | 1 | 0 | 9 |
| 6-C | 80 | 4 | 4 | 2 | 2 | 1 | 13 |
| 6-C | 100 | 4 | 4 | 2 | 2 | 1 | 13 |
| 18-O | 110 | 4 | 4 | 0 | 0 | 0 | 8 |
| 11-P | 115 | 4 | 4 | 3 | 3 | 2 | 16 |
| 20-W | 130 | 4 | 4 | 2 | 1 | 1 | 12 |
| 26-C | 130 | 4 | 3 | 3 | 1 | 0 | 11 |
| 12-P | 140 | 4 | 4 | 4 | 3 | 2 | 17 |
| 27-McG | 165 | 4 | 2 | 2 | 1 | 0 | 9 |
| 8-R | 200 | 4 | 3 | 2 | 1 | 1 | 11 |
| 12-P | 220 | 4 | 4 | 4 | 1 | 0 | 13 |
| 28-J | 240 | 4 | 4 | 3 | 2 | 2 | 15 |
| 21-H | 270 | 4 | 4 | 3 | 2 | 2 | 15 |
| 29-A | 280 | 4 | 4 | 3 | 2 | 2 | 15 |
| 11-P | 310 | 3 | 2 | 1 | 0 | 0 | 6 |
| 21-H | 330 | 4 | 4 | 4 | 3 | 3 | 18 |
| 8-R | 345 | 4 | 4 | 3 | 2 | 1 | 14 |
| 8-R | 350 | 4 | 3 | 3 | 1 | 0 | 11 |
| 11-P | 370 | 4 | 2 | 2 | 0 | 0 | 8 |
| 12-P | 400 | 4 | 4 | 3 | 1 | 0 | 12 |
| 27-McG | 430 | 4 | 3 | 2 | 1 | 0 | 10 |
| 7-P | 500 | 3 | 3 | 3 | 2 | 1 | 12 |
| 21-H | 555 | 4 | 3 | 3 | 3 | 2 | 15 |
| 29-A | 570 | 4 | 4 | 2 | 1 | 1 | 12 |
| 8-R | 585 | 4 | 4 | 3 | 2 | 1 | 14 |
| 29-A | 600 | 4 | 4 | 3 | 3 | 2 | 16 |
| 12-P | 610 | 4 | 2 | 0 | 0 | 0 | 6 |
| 4-H | 640 | 4 | 2 | 2 | 1 | 0 | 9 |
| 1-A | 650 | 4 | 3 | 3 | 3 | 3 | 16 |
| 16-B | 680 | 4 | 4 | 3 | 2 | 1 | 14 |
| 3-A | 760 | 3 | 2 | 0 | 0 | 0 | 5 |
| 11-P | 800 | 4 | 2 | 1 | 0 | 0 | 7 |
| 4-H | 850 | 2 | 2 | 1 | 1 | 0 | 6 |
| 6-C | 900 | 3 | 3 | 2 | 2 | 0 | 10 |
| 19-F | 960 | 4 | 3 | 2 | 1 | 0 | 10 |
| 21-H | 995 | 4 | 4 | 4 | 3 | 0 | 15 |
| 14-S | 1,040 | 4 | 3 | 2 | 1 | 0 | 10 |
| 26-C | 1,110 | 4 | 4 | 3 | 2 | 2 | 15 |
| 26-C | 1,165 | 4 | 4 | 2 | 1 | 0 | 11 |
| 28-J | 1,170 | 4 | 4 | 3 | 1 | 1 | 13 |
| 2-W | 1,290 | 3 | 3 | 2 | 2 | 1 | 11 |
| 9-J | 1,300 | 4 | 3 | 1 | 0 | 0 | 8 |
| 26-C | 1,340 | 4 | 3 | 2 | 0 | 0 | 9 |
| 5-M | 1,350 | 4 | 3 | 3 | 2 | 1 | 13 |
| 4-H | 1,350 | 3 | 3 | 1 | 1 | 0 | 8 |
| 8-R | 1,570 | 4 | 4 | 4 | 3 | 3 | 18 |
| 3-A | 1,665 | 4 | 4 | 3 | 3 | 3 | 17 |
| 3-A | 1,670 | 4 | 4 | 3 | 2 | 0 | 13 |
| 19-F | 1,740 | 4 | 4 | 3 | 1 | 0 | 12 |
| 16-B | 1,820 | 4 | 4 | 3 | 2 | 0 | 13 |
| 5-M | 1,960 | 4 | 2 | 2 | 1 | 0 | 9 |
| 2-W | 2,000 | 4 | 4 | 4 | 3 | 3 | 18 |
| 28-J | 2,005 | 4 | 3 | 2 | 1 | 0 | 10 |
| 3-A | 2,100 | 4 | 4 | 4 | 3 | 2 | 17 |
| 29-A | 2,140 | 4 | 4 | 2 | 2 | 1 | 13 |
| 12-P | 2,270 | 2 | 0 | 0 | 0 | 0 | 2 |
| 12-P | 2,400 | 3 | 3 | 2 | 0 | 0 | 8 |
| 6-C | 2,590 | 3 | 3 | 2 | 2 | 0 | 10 |
| 1-A | 2,650 | 4 | 3 | 1 | 0 | 0 | 8 |
| 9-J | 3,250 | 4 | 4 | 3 | 1 | 0 | 12 |
| 12-P | 4,000 | 4 | 3 | 1 | 0 | 0 | 8 |
| 12-P | 4,900 | 4 | 3 | 2 | 0 | 0 | 9 |
| 8-R | 6,150 | 4 | 4 | 4 | 3 | 3 | 18 |
| 28-J | 6,680 | 4 | 4 | 2 | 1 | 1 | 12 |
| 7-P | 9,200 | 4 | 2 | 0 | 0 | 0 | 6 |
| 15-W | 13,600 | 3 | 2 | 0 | 0 | 0 | 5 |

the fact that in the low dilutions used enough milk solids were added to increase the nutrient quality of the agar. Our tables were therefore made from the results on plain nutrient agar.

Eighty-five individual samples from twenty-three wetnurses were examined to determine the relationship between the bacterial count of their fresh milk and its lysozyme content. Table 5 shows the constant presence of lysozyme, the lytic index and the bacterial count of the eighty-five freshly collected specimens. From one to eight samples of breast milk, collected on different days from each of the twenty-three women, were used.

The figures in the second column are arranged in increasing order of bacterial count. The next five columns show the degree of lysis of the same sample, tested in each of the five dilutions. A comparison of the data in the second column with those in the next five fails to

TABLE 6.—*Average Bacterial Counts and Lysozyme Content of Eighty-Five Samples of Human Milk, Freshly Obtained and Manually Expressed*

| No. of Samples | Average Bacterial Counts | Average Lysis at Various Dilutions | | | | | Average Lytic Index |
|---|---|---|---|---|---|---|---|
| | | 1:1.1 | 1:10 | 1:100 | 1:1,000 | 1:10,000 | |
| 22 | 0- 100 | 4 | 4 | 3 | 2 | 1 | 14 |
| 33 | 110- 995 | 4 | 3 | 2 | 1 | 1 | 11 |
| 16 | 1,040- 2,000 | 4 | 3 | 3 | 2 | 1 | 13 |
| 14 | 2,005-13,600 | 4 | 3 | 2 | 1 | 0 | 10 |

show any relationship between the immediate bacterial count and the lysozyme content of the manually expressed fresh milk. The figures in the last column are the lytic indexes, computed as previously described, which may be used for comparison throughout the paper.

Table 6 is a consolidated average of table 5 showing the relationship between the lytic index and the bacterial count. Although the lytic index is lowest in the samples of milk averaging the highest bacterial counts and highest in those with the lowest bacterial counts, an examination of this relationship for the intermediate groups discloses a reversal of figures. From these statistics, it would seem reasonable to conclude that the bacterial count of the fresh milk was not dependent on the lytic index alone.

To determine the effect of keeping raw human milk, fresh individual samples were placed in the refrigerator at a temperature of from 9 to 12 C. after the immediate inoculation of plates for bacterial counts and titrations for lysozyme. The making of counts and titrations for the samples was repeated on one or more of the succeeding four days.

In beginning the study of our problem, we assumed from Schlaeppi's report [6] that the rise or fall in the bacterial count of refrigerated breast milk would be a sufficient index of the lytic power of a given specimen.

Titrations against sarcinas, therefore, were not made on a few specimens the bacterial counts for which are recorded in table 7.

In tabulating results, the specimens of milk were divided into groups I, II and III, according to their original lytic indexes of 14 to 18, 10

TABLE 7.—*Effect of Keeping Raw Human Milk (at a Temperature of from 9 to 12 C.) on the Bacterial Count and the Lytic Index*

| | Immediate | | After 24 Hours | | | After 48 Hours | | | After 72 Hours | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Group | Lytic Index | Bacterial Count* | Lytic Index | Bacterial Count | Percentage of Change from First Bacterial Count | Lytic Index | Bacterial Count | Percentage of Change from First Bacterial Count | Lytic Index | Bacterial Count | Percentage of Change from First Bacterial Count |
| I | 16 | 650 | .. | 700 | + 7 | 14 | 100 | — 84 | .. | ..... | ..... |
| (15 | 18 | 1,000 | .. | 300 | — 70 | 14 | 950 | — 5 | .. | 300 | — 70 |
| samples) | 17 | 1,665 | .. | 1,050 | — 37 | 12 | 700 | — 57 | .. | 800 | — 52 |
| | 16 | 115 | 5 | 135 | + 16 | .. | 130 | + 13 | .. | ..... | ..... |
| | 15 | 1,820 | .. | 760 | — 58 | .. | ..... | ..... | .. | ..... | ..... |
| | 15 | 555 | 13 | 60 | — 89 | 18 | 190 | — 66 | 16 | 60 | — 90 |
| | 15 | 270 | 11 | 0 | —100 | 15 | 160 | — 41 | 13 | 205 | — 24 |
| | 15 | 995 | 16 | 20 | — 97 | 18 | 60 | — 94 | 16 | 20 | — 97 |
| | 18 | 6,150 | 18 | 4,040 | — 34 | 14 | 2,420 | — 60 | 14 | 2,725 | — 55 |
| | 18 | 1,570 | 16 | 670 | — 57 | 18 | 330 | — 79 | 16 | 290 | — 81 |
| | 14 | 585 | 18 | 250 | — 57 | 16 | 150 | — 74 | 18 | 20 | — 96 |
| | 14 | 345 | 18 | 85 | — 75 | 16 | 70 | — 79 | 17 | 10 | — 97 |
| | 15 | 246 | 15 | 0 | —100 | 15 | 0 | —100 | 15 | 0 | —100 |
| | 15 | 280 | 10 | 95 | — 66 | 12 | 130 | — 53 | 11 | 135 | — 52 |
| | 16 | 600 | 12 | 590 | — 1 | 14 | 265 | — 56 | 11 | 210 | — 65 |
| Average | 15.8 | 1,123 | 13.8 | 584 | — 54 | 15 | 404 | — 59 | 14.7 | 398 | — 73 |
| II | 11 | 1,290 | 8 | 900 | — 30 | .. | 1,450 | + 12 | .. | ..... | ..... |
| (13 | 13 | 1,670 | .. | 195 | — 88 | .. | ..... | ..... | .. | 680 | — 59 |
| samples) | 10 | 2,590 | 5 | 1,650 | — 36 | 9 | 865 | — 67 | .. | ..... | ..... |
| | 12 | 500 | 14 | 200 | — 60 | 13 | 400 | — 20 | 4 | 600 | + 20 |
| | 11 | 200 | 11 | 650 | +225 | 10 | 300 | + 50 | 11 | 600 | +200 |
| | 11 | 1,040 | .. | 1,340 | + 29 | .. | ..... | ..... | .. | ..... | ..... |
| | 13 | 100 | 18 | 0 | —100 | 17 | 0 | —100 | 16 | 10 | — 90 |
| | 10 | 2,005 | 13 | 1,755 | — 12 | 11 | 590 | — 70 | 14 | 545 | — 72 |
| | 13 | 1,170 | 13 | 860 | — 26 | 9 | 295 | — 74 | 10 | 830 | — 29 |
| | 12 | 6,680 | 14 | 3,250 | — 51 | 13 | 420 | — 93 | 13 | 820 | — 87 |
| | 13 | 2,140 | 14 | 3,550 | + 66 | 10 | 2,475 | + 16 | 10 | 2,435 | + 14 |
| | 13 | 100 | 18 | 0 | —100 | 17 | 0 | —100 | 16 | 10 | — 90 |
| | 12 | 570 | 12 | 680 | + 19 | 14 | 230 | — 59 | 13 | 305 | — 46 |
| Average | 11.8 | 1,543 | 12.6 | 1,159 | — 14 | 12.3 | 639 | — 47 | 11.9 | 683 | — 24 |
| III | 8 | 2,650 | 8 | 550 | — 79 | 7 | 520 | — 80 | .. | ..... | ..... |
| (10 | 5 | 760 | .. | 380 | — 50 | 7 | 4,035 | +430 | .. | ..... | ..... |
| samples) | 8 | 1,300 | 8 | 990 | — 23 | 16 | 600 | — 54 | 7 | 3,500 | +169 |
| | 7 | 800 | 9 | 650 | — 18 | .. | 525 | — 34 | 8 | 400 | — 50 |
| | 8 | 370 | 8 | 380 | + 3 | .. | ..... | ..... | .. | ..... | ..... |
| | 6 | 310 | .. | 1,200 | +287 | .. | ..... | ..... | .. | 375 | + 21 |
| | 6 | 610 | 8 | 340 | — 44 | .. | 530 | — 13 | 7 | 210 | — 65 |
| | 9 | 1,350 | 9 | 700 | — 48 | 11 | 1,900 | + 40 | 6 | 700 | — 48 |
| | 9 | 1,960 | .. | 3,500 | + 78 | 9 | 12,000 | +512 | .. | ..... | ..... |
| | 9 | 4,900 | 9 | 3,625 | — 26 | .. | ..... | ..... | .. | ..... | ..... |
| Average | 7.5 | 1,501 | 8 | 1,232 | + 8 | 10 | 2,873 | +114 | 7 | 1,037 | + 5 |

* As explained in the text the bacterial counts shown are averages of those for the cultures made with 1:10 and with the 1:100 dilutions.

to 13 and 5 to 9, inclusive (table 7). The results of the examination of all specimens with original bacterial counts of 100 or more are recorded. Seven counts fell below this figure and are not included in table 7.

In group I, fourteen of fifteen specimens refrigerated for from twenty-four to seventy-two hours showed a marked decrease in bacterial count; one increased. For the group there was an average decrease from the original count of 54 per cent at the end of twenty-four hours, 59 per cent in forty-eight hours and 73 per cent in seventy-two hours.

In group II, five of thirteen specimens increased in bacterial count when refrigerated for from twenty-four to seventy-two hours; eight decreased. The group averaged a 14 per cent increase above the original count at the end of twenty-four hours, a 47 per cent decrease in forty-eight hours and a 25 per cent decrease in seventy-two hours.

In group III, five of ten specimens showed an increase when refrigerated for from twenty-four to seventy-two hours; five showed a decrease. The group averaged an 8 per cent increase above the original count at the end of twenty-four hours, a 114 per cent increase in forty-eight hours and a 5 per cent increase in seventy-two hours. The seventy-two hour figure (5 per cent) we believe to be statistically too low, as the data were insufficient; the two specimens of milk which showed the highest bacterial count at the end of forty-eight hours were not reexamined at seventy-two hours and were therefore not tabulated. A trend noted (table 7) was that when an increase above the first count occurred in twenty-four hours it tended to continue to the end of the forty-eight and seventy-two hour periods. Also there was little tendency for counts to change from a decrease to an increase.

A discrepancy was seen between the lytic index as determined when a suspension of sarcinas was used and the bactericidal action of the milk on the natural organisms in a few of the specimens. It may be explained by analogy from the fact, demonstrated by Schlaeppi,[7] that the activity of a bacteria-free filtrate of any mother's milk is greater against organisms cultured from her own secretion than against like organisms from an abscess in her body or against similar strains of staphylococci from the milk of another woman. Sarcinas—foreign organisms—likewise may be unaffected by lysozyme in some instances.

The samples of milk placed according to their primary lytic indexes (from 14 to 18) in group I (table 7) showed a decrease in bacterial count greater than that in group II. This held true at the end of twenty-four, of forty-eight and of seventy-two hours. The specimens in group II, with lytic indexes ranging from 10 to 13, showed decrease in bacterial count, but the specimens in group III, with lytic indexes of from 5 to 9, showed an increase. From these facts it may be assumed that the lysozyme of human milk is a bacteriolytic factor and that the low bacterial counts observed in specimens of such milk when it is kept at from 9 to 12 C. are in direct proportion to the amount of lysozyme present in the specimens. It is therefore safe to preserve aseptically

collected raw human milk in a refrigerator for seventy-two hours and then use it for infant feeding.

Seventy-nine specimens were tabulated for the purpose of determining the lysozyme content of mothers' milk during the different months of lactation. The average lytic indexes ranged from 9 to 16. There was no regular curve of rise or fall in the lytic index during successive months of lactation in this series (table 8).

In investigating the methods of expression of human milk under aseptic conditions, manual expression, the hand breast pump and the electric breast pump were used. The use of the electric or the hand pump permits boiling of all parts through which milk flows into the container. The employment of either pump necessitates pouring from the reservoir into sterile containers. The pumps of each type were frequently examined bacteriologically before use and always found sterile.

TABLE 8.—*Average Lytic Indexes of Fresh Human Milk, Manually Expressed, in Various Months of Lactation*

| | Months | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
| Number of specimens..... | 7 | 17 | 5 | 12 | 5 | 4 | 5 | 5 | 6 | 7 | 5 | 1 |
| Average lytic index..... | 12 | 12 | 10 | 13 | 9 | 10 | 12 | 14 | 12 | 11 | 16 | 12 |

Table 9 shows the lytic indexes and plate counts of milk collected by manual expression, electric pump and hand pump. Wetnurses H.-4, P.-7 and O.-16 were milked at one sitting by each of the three methods in turn. Wetnurses A., C., R. and Ch., however, were milked at each of three sittings by a different one of the three methods. Seven wetnurses were utilized on fifteen occasions.

The milk from each of four women (A., C., R. and Ch.) was separated, as obtained, into four 1 ounce portions. The term "portion" is used to designate the part of the breast milk examined. Milking was divided into four periods, and one portion was collected during each period. This method renders more certain a uniformity of bacterial count and lytic index of samples.

The lytic indexes were higher with manual expression than with the electric pump in twelve and than with the hand pump in fourteen of nineteen specimens examined. The lytic index was lower with manual expression than with the electric pump in four and than with the hand pump in one instance. For seven of the nineteen specimens two of the methods gave identical lytic indexes. For two of these seven specimens all three methods gave the same lytic index.

The lytic index was generally higher when manual expression was used than when the milk was obtained by mechanical means. In view of the fact previously demonstrated that bacterial count was reduced as the lytic index increased consideration must be given to the method of expression of the milk if collected for general use.

The bacterial count made almost immediately after collection of the samples of milk yielded a surprising result. The milk obtained by manual expression had the lowest count in thirteen, that obtained with

TABLE 9.—*Effect of Manual Expression, the Electric Pump and the Hand Pump on the Lytic Index and the Bacterial Count of Human Milk* *

| | | Lytic Index | | | Bacterial Count | | |
|---|---|---|---|---|---|---|---|
| Wet-nurse | Milk, 1 Oz. Portion | Manual Expression | Electric Pump | Hand Pump | Manual Expression | Electric Pump | Hand Pump |
| H.-4 | | 8 | 8 | 8 | 700 | 6,600 | 2,100 |
| P.-7 | | 6 | 6 | 8 | 9,200 | 40,000 | 62,500 |
| O.-16 | | 8 | 6 | 4 | 120 | 142,400 | 3,100 |
| A. | First | 13 | 11 | 13 | 2,140 | 350 | 31,330 |
| | Second | 12 | 12 | 12 | 570 | 1,480 | 19,700 |
| | Third | 15 | 8 | 13 | 280 | 1,535 | 16,600 |
| | Last | 16 | 12 | 14 | 600 | 485 | 8,500 |
| C. | First | 18 | 15 | 12 | 10 | 2,930 | 30 |
| | Second | 18 | 11 | 10 | 0 | 760 | 60 |
| | Third | 13 | 11 | 11 | 100 | 220 | 130 |
| | Last | 13 | 15 | 11 | 80 | 700 | 60 |
| R. | First | 18 | 8 | 8 | 6,150 | 24,900 | 1,140 |
| | Second | 18 | 10 | 8 | 1,570 | 26,700 | 470 |
| | Third | 14 | 12 | 8 | 585 | 10,300 | 780 |
| | Last | 14 | 11 | 7 | 345 | 8,000 | 3,230 |
| Ch. | First | 14 | 18 | 12 | 0 | 130 | 390 |
| | Second | 14 | 18 | 9 | 0 | 300 | 460 |
| | Third | 14 | 11 | 10 | 0 | 380 | 260 |
| | Last | 11 | 17 | 11 | 1,165 | 6,900 | 380 |
| | Average | 13.4 | 11.6 | 9.9 | 1,242 | 14,477 | 7,959 |

* The lytic index was obtained and plate cultures were prepared almost immediately—always within an hour after the milk was expressed. Specimens were collected in iced containers. Each of the first three specimens was taken from all the milk obtained at one sitting. Each of the other specimens was taken from the portion of milk expressed during one of four periods into which the sitting was divided.

the hand pump in four and that obtained with the electric pump in two of the nineteen specimens examined. An explanation of these results was apparent when the mechanics of the three methods were observed. A large area of breast tissue, which had been cleansed by the usual method, was bathed in milk by the use of the mechanical apparatus, and the milk was thereby constantly inoculated by bacteria from the skin. In using manual expression the stream of milk flowed directly into a sterile container, and no opportunity for such contamination occurred.

It was important to determine what difference existed between the lytic index and the bacterial count for various portions of breast milk

collected by any method, in order to decide whether any portion ought to be discarded or to be boiled before it was used.

Table 10 shows the results of the examination of each of four portions of milk obtained by manual expression. Similarly, table 11 shows

TABLE 10.—*Lytic Indexes and Bacterial Counts for Portions of Human Milk Manually Expressed*

| | First Ounce | | Second Ounce | | Third Ounce | | Last Ounce | |
|---|---|---|---|---|---|---|---|---|
| Wetnurse | Lytic Index | Bacterial Count | Lytic Index | Bacterial Count | Lytic Index | Bacterial Count | Lytic Index | Bacterial Count |
| H.-21 | 15 | 555 | 18 | 330 | 15 | 270 | 15 | 995 |
| R.-8 | 18 | 6,150 | 18 | 1,570 | 14 | 585 | 14 | 345 |
| J. J.-28 | 15 | 240 | 10 | 2,005 | 13 | 1,170 | 12 | 6,680 |
| A.-29 | 13 | 2,140 | 12 | 570 | 15 | 280 | 16 | 600 |
| P.-12 | 8 | 2,400 | 12 | 400 | 13 | 220 | 17 | 140 |
| McG.-27 | 11 | 50 | 9 | 70 | 9 | 165 | 10 | 430 |
| Ch.-26 | 15 | 1,110 | 11 | 130 | 8 | 40 | 9 | 1,340 |
| Average | 13.5 | 1,806 | 12.9 | 725 | 12.4 | 390 | 13.3 | 1,504 |

TABLE 11.—*Lytic Indexes and Bacterial Counts for Portions of Human Milk Obtained with an Electric Pump*

| | First Ounce | | Second Ounce | | Third Ounce | | Last Ounce | |
|---|---|---|---|---|---|---|---|---|
| Wetnurse | Lytic Index | Bacterial Count | Lytic Index | Bacterial Count | Lytic Index | Bacterial Count | Lytic Index | Bacterial Count |
| J. J.-28 | 10 | 7,980 | 13 | 860 | 9 | 440 | 8 | 970 |
| A.-29 | 11 | 350 | 12 | 1,480 | 8 | 1,535 | 12 | 485 |
| J. J.-28 | 8 | 9,175 | 10 | 13,100 | 10 | 23,400 | 14 | 6,370 |
| Co.-30 | 12 | 2,575 | 10 | 2,040 | 14 | 3,680 | 12 | 5,040 |
| J.-9 | 10 | 17,600 | 12 | 5,400 | 10 | 4,300 | 15 | 5,900 |
| R.-8 | 8 | 24,900 | 10 | 26,700 | 12 | 10,300 | 11 | 8,000 |
| C.-6 | 15 | 2,930 | 11 | 760 | 11 | 220 | 15 | 700 |
| Ch.-26 | 18 | 130 | 18 | 300 | 11 | 380 | 17 | 6,900 |
| Average | 11.5 | 8,205 | 12 | 6,330 | 10.6 | 5,532 | 13 | 4,295 |

TABLE 12.—*Lytic Indexes and Bacterial Counts for Portions of Human Milk Obtained with a Hand Pump*

| | First Ounce | | Second Ounce | | Third Ounce | | Last Ounce | |
|---|---|---|---|---|---|---|---|---|
| Wetnurse | Lytic Index | Bacterial Count | Lytic Index | Bacterial Count | Lytic Index | Bacterial Count | Lytic Index | Bacterial Count |
| Ch.-26 | 12 | 390 | 9 | 460 | 10 | 260 | 11 | 380 |
| Sc.-14 | 14 | 60 | 13 | 130 | 12 | 160 | 14 | 40 |
| A.-29 | 13 | 31,300 | 12 | 19,700 | 13 | 16,600 | 14 | 8,500 |
| Sc.-14 | 17 | 250 | 14 | 90 | 16 | 340 | 13 | 205 |
| C.-6 | 12 | 30 | 10 | 60 | 11 | 130 | 11 | 60 |
| Sc.-14 | 13 | 30 | 11 | 440 | 9 | 40 | 10 | 160 |
| P.-12 | 7 | 15,300 | 7 | 3,410 | 5 | 3,700 | 7 | 4,850 |
| R.-8 | 8 | 1,140 | 8 | 470 | 8 | 780 | 7 | 3,230 |
| Average | 12 | 6,062 | 10.5 | 3,095 | 10.5 | 2,751 | 10.8 | 2,178 |

these results when the electric pump was used, and table 12, the results with the hand pump.

It will be noted from these three tables that the average bacterial count from the first portion is greater than the average count from

the succeeding portions. This apparent difference cannot be regarded as significant, as fifteen of the twenty-three wetnurses showed in some portion subsequent to the first a bacterial count greater than that initially recorded.

None of the milk collected by manual expression had a count high enough to appear dangerous, and all portions were fed raw with no ill result. The wetnurses preferred manual expression to the other methods because it was more comfortable and more productive. The milk obtained by hand pump was fed raw, but that collected by electric pump was boiled before using.

The lytic indexes of the various portions collected showed no striking differences (tables 10, 11 and 12).

The predominating bacterium found in the samples of milk cultured in this research was Staph. albus. Frequently, hemolytic staphylococci were found, and the milk containing them was fed raw to premature infants without untoward results. Streptococci were never found. No epidemic of diarrhea occurred in the wards during the progress of this study. Raw milk was fed by choice to premature infants who had soft or frequent stools while they were on other diets. Detailed results will be reported later.

## COMMENT

It is a truism that for reduction of the mortality of infants, especially premature infants, human milk is invaluable.

The present study deals with the factors affecting the bacterial count of expressed human milk and was undertaken to determine whether such milk might be safely fed raw to infants and particularly to premature infants. Both lysozyme and the indigenous bacteria are destroyed by boiling. It seems desirable to preserve these elements. This can be done only if the milk is fed in the raw state.

Wetnurses were carefully selected for quantity of milk and physical health. They were examined physically and tested serologically. Their milk was examined bacteriologically to determine what were the prevailing organisms, including hemolytic streptococci. Smears of material from the pharynx were made on hemolytic plates.

The breasts were made surgically clean, and the milk was collected by aseptic technic. We have shown that the bacterial count is dependent on careful preparation of the breasts and on the method of expression and that if the milk is expressed manually the bacterial count is initially low. Furthermore, we have shown that holding human milk in a refrigerator for as long as seventy-two hours does not increase the bacterial count significantly. The fact that the low initial count does not show an important increase is evidence of the high lysozyme content of breast milk. In our opinion, there is an advantage in implanting the

normal gram-positive bacillus of breast milk in those infants who must be sustained by human milk. This can be done by using the milk in its raw state.

We believe that one of the important factors in the reduction of the mortality of premature infants at the Cook County Hospital has been the feeding of raw milk, collected as here described. Breast milk not conforming to the requirements laid down in making this study should be boiled before using.

## SUMMARY AND CONCLUSIONS

Lysozyme exists as an active bacteriolytic agent in human milk and is greatly reduced by boiling. It varies in amount.

In the presence of adequate amounts of lysozyme, the bacterial count of milk kept at 9 to 12 C. for from twenty-four to seventy-two hours is lower than that initially recorded.

The higher the initial lytic index (table 7), the greater is the reduction in the bacterial count during refrigeration.

Staph. albus was the predominating organism observed.

In confirmation of the observations of Schlaeppi, manual expression of breast milk was proved preferable. Milk obtained by that method has a lower bacterial count than milk collected by means of a hand-operated or an electric breast pump.

The lysozyme content apparently is not influenced by the duration of the period of lactation between the second week and the twelfth month.

The lytic index did not vary significantly in the different portions of milk obtained from one woman at a single sitting.

Hence it would appear, according to the facts presented in this study, that raw milk with a bacterial count of less than 10,000 per cubic centimeter which has been obtained under aseptic precautions from women free from tuberculosis, syphilis and acute infections and having normal breasts may be pooled, kept in a refrigerator for from twenty-four to seventy-two hours and safely fed to premature or young infants.

185 North Wabash Avenue.

# IRON VERSUS IRON AND COPPER IN THE TREATMENT OF ANEMIA IN INFANTS

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AND

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Although the supplementary value of copper with iron as a necessary catalytic agent in the formation of hemoglobin in experimental animals is generally accepted, some investigators feel that this has not been proved satisfactorily for infants. Since we found that approximately 21 per cent of the infants brought to the child health centers of Madison, Wis., during the past year tended to become anemic during their first year of life, the problem of the most efficacious method of treating anemia seems to be one of utmost importance.

This report compares the effect of iron alone as a therapeutic agent with that of iron supplemented with copper. In a recent paper, Elvehjem, Siemers and Mendenhall [1] showed that iron plus copper therapy caused an increase in the hemoglobin content of the blood from between 9 and 11 Gm. to 12 and 13.5 Gm. per hundred cubic centimeters. However, Mackay [2] reported that the copper supplement is of no benefit and that babies respond as well to iron alone as they do to iron fortified with copper. Gorter [3] and Sheldon [4] referred to the probability that the anemia of infants is influenced by other factors than those concerned in the anemia of animals.

Vaughan [5] stated in her book on the anemias that "copper is worthy of trial in any case that does not respond to iron, but such cases appear

From the Department of Agricultural Chemistry, University of Wisconsin.

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1. Elvehjem, C. A.; Siemers, A., and Mendenhall, D. R.: Effect of Iron and Copper Therapy on Hemoglobin Content of the Blood of Infants, Am. J. Dis. Child. **50**:28 (July) 1935.

2. Mackay, H. M. M.: Copper in Treatment of Nutritional Anemia in Infancy, Arch. Dis. Childhood **8**:145, 1933.

3. Gorter, E.: Copper and Anemia, Am. J. Dis. Child. **46**:1066 (Nov.) 1933.

4. Sheldon, J. H.: The Mineral Basis of Life, Brit. M. J. **1**:47 (Jan. 13) 1934.

5. Vaughan, J. M.: The Anemias, London, Oxford University Press, 1934.

to be rare." Marriott [6] expressed the belief that recovery from anemia may be hastened by giving copper to supplement the iron, but he stated that small amounts should be added for only short periods of time. As a maximum dose he suggested 1 mg. of copper per kilogram of body weight per day. If liver, oatmeal and whole wheat are introduced into the diet at a sufficiently early age it is unlikely, in his opinion, that there will be a copper deficiency.

According to the papers published recently, evidence seems to indicate that copper is necessary in order that one may obtain an optimum hemoglobin response in infants. Although this evidence may be considered somewhat scanty, several studies have been reported which represent an accumulation of a large number of data. Usher, MacDermot and Lozinski [7] made observations on 233 infants in an institution for foundlings. Normal children were observed for an average period of nine months. The control group received the same adequate diet as was fed to the other two groups, one of which received iron as a medication and the other iron plus copper. In the infants given iron alone, the hemoglobin content reached, on an average, a level 15 per cent higher at 1 year of age than that attained by the control group. In those given supplemental copper, the hemoglobin content showed a 19 per cent increase. The copper also produced advantageous results by increasing the resistance to infections, bringing about a better gain in weight and reducing the mortality rate, which was 14.5 per cent for the control children, 11.6 per cent for the group receiving iron alone and 6.3 per cent for those given the additional copper.

Goldstein [8] studied 86 children with simple secondary anemia at an orphan asylum. His studies continued for over two years, each child being observed for at least several months. Diets well balanced as to calories, vitamins and minerals were fed, and iron plus various catalysts were given in an attempt to correct the anemic condition. He found that a combination of iron plus copper and vitamin B produced the optimum increase in the hemoglobin content.

In the report published by Elvehjem and others,[1] they showed that there is a definitely positive hemoglobin response to the administration of iron and copper in anemic infants. The average hemoglobin level of children receiving iron and copper was considerably higher than that of children who were untreated, and the response was found to

6. Marriott, W. M.: Infant Nutrition, ed. 2, St. Louis, C. V. Mosby Company, 1935.

7. Usher, S. J.; MacDermot, P. N., and Lozinski, E.: Prophylaxis of Simple Anemia in Infancy with Iron and Copper, Am. J. Dis. Child. **49**:642 (March) 1935.

8. Goldstein, H.: Uses of Iron and Iron Catalysts in Simple Anemia of Children, Arch. Pediat. **52**:234 (April) 1935.

be particularly rapid in the infants suffering from severe nutritional anemia. Since the values for almost all healthy infants not receiving therapy were lower than those for treated anemic infants, the significance of the slight anemia prevalent among small children was questioned. The paper of Usher and his co-workers [7] tends to remove all doubt as to the relation between the low hemoglobin content of the blood and the health of the infant.

Analyses of infant cadavers have revealed that smaller amounts of copper are found in the livers of anemic infants than in those of nonanemic infants.[9] Since this is true, supplemental copper seems to be logically indicated. Also the copper content in young growing tissues is richer than in adult tissues, which suggests that copper may be directly associated with growth.

Since milk is low in both iron and copper, 1 liter of certified milk containing from 0.12 to 0.18 mg. of copper and approximately 0.50 mg. of iron, it is not surprising that the reserves of infants may become depleted and that anemia may result. While copper is present in all living matter in varying amounts, which is an indication that it is essential for animal and plant growth, the diet of the infant is so limited that even traces of it may not be supplied. Liver, oatmeal and whole wheat contain appreciable though small amounts of the element; the copper content of cow's milk is increased when the milk is pasteurized, evaporated or dried in receptacles of copper or its alloys.

## EXPERIMENTS

The data presented in this paper were obtained at three of the child health centers of the Madison Public Health Nursing Association. Samples of blood were taken between 2 and 4 in the afternoon. The Newcomer method was used to determine the hemoglobin values. Determinations were made for practically all the babies brought to the clinics. Those whose hemoglobin content proved to be within the normal range were examined periodically, usually about once every four weeks. Anemic children had their blood tested at more frequent intervals, every two or three weeks if the parents cooperated and brought them to the clinic at the specified times. At least two readings were made before any therapy was started. Some of the anemic infants were given iron alone in the form of ferric pyrophosphate, $Fe_4(P_2O_7)_3$. Others were given the ferric pyrophosphate supplemented with copper sulfate, $CuSO_4$. To obtain a true comparison of the effectiveness of additional copper, iron alone was given first and the iron fortified with copper was given later to the same child. This procedure was followed with 32 of the 160 children with anemia studied.

The solution of iron was prepared by dissolving 16 Gm. of powdered ferric pyrophosphate in 400 cc. of distilled water containing 5 per cent of alcohol. One teaspoonful (5 cc.) was the daily dose; it is equivalent to 25 mg. of elemental iron.

9. Chou, T. P., and Adolph, W. H.: Copper Metabolism in Man, Biochem. J. **29**:476 (Feb.) 1935.

Ferric pyrophosphate was used because it has been found to be readily available.[10] It is easily soluble, practically tasteless and odorless and has no astringent properties. It is also low in cost. Owing to the fact that it will not precipitate in a neutral solution, it is probably available to the body even in cases of achlorhydria. Faber and his associates[11] reported that of 10 patients between 7 months and 2 years of age who were suffering from nutritional iron deficiency anemia, 6 showed a complete absence of free acid in the gastric juice and 4 a low amount. It was concluded that the reduction in the amount of acid present is a possible causative factor in the prevalence of hypochromic anemia in childhood. Seemingly, there is difficulty in absorbing iron from the ordinary diet. Therefore, it is extremely important to give medicinal iron in a form which will not precipitate in the absence of acid.

For the iron and copper solution, 0.32 Gm. of copper sulfate was added to the formula previously mentioned. This gave the equivalent of 1 mg. of elemental copper per five cubic centimeters. In all cases the mother was advised to incorporate the medicinal preparation in the child's milk or orange juice.

Previous work[1] has shown the ratio of 1 mg. of copper to 25 mg. of iron to be the most satisfactory. Also, it has shown that if the elements are given in a readily available form these amounts are adequate to cure nutritinoal anemia in infants. It seems dangerous to administer large amounts of iron, as suggested by some workers, since animal experiments have pointed to the fact that excess iron interferes seriously with the assimilation of phosphorus and may produce rickets.[12] If the level of iron is sufficient for the iron in the organism to unite with one-half the total phosphorus in the diet as ferrous phosphate ($FePO_4$), the bone ash is thereby reduced to from 25 to 27 per cent. There seems to be no advantage to the administration of more than 1 mg. of copper daily, although larger amounts have been given by some workers.[13] The toxic effects of excessive amounts are known to be accumulative.

Individual records and graphs were kept for all the anemic children studied to whom iron or iron and copper was being administered. The healthy nonanemic children who were receiving no therapy were classified in age groups of four weeks, such as from 4 to 8 weeks and from 8 to 12 weeks. The hemoglobin level at the various ages was charted and averaged in an effort to substantiate the average curve for normal children which was reported in 1933.[14]

## RESULTS

The results of the study on normal, healthy children indicate that the hemoglobin curve previously established can be verified by repeti-

10. Elvehjem, C. A.; Hart, E. B., and Sherman, W. C.: Availability of Iron from Different Sources for Hemoglobin Formation, J. Biol. Chem. **103**:61 (Nov.) 1933.

11. Faber, H. K.; Mermod, C.; Gleason, A. L., and Watkins, R. P.: Microcytic Hypochromic Anemia in Infancy and Childhood, J. Pediat. **7**:435 (Oct.) 1935.

12. Deobald, H. J., and Elvehjem, C. A.: Effects of Feeding High Amounts of Soluble Iron and Aluminum Salts, Am. J. Physiol. **111**:118 (Feb.) 1935.

13. Cason, J. F.: Use of Copper and Iron in the Treatment of Secondary Anemia in Children, J. Pediat. **4**:614 (May) 1934. Josephs, H. W.: Treatment of Anemia of Infancy with Iron and Copper, Bull. Johns Hopkins Hosp. **49**:246 (Oct.) 1931.

14. Elvehjem, C. A.; Peterson, W. H., and Mendenhall, D. R.: Hemoglobin Content of the Blood of Infants, Am. J. Dis. Child. **46**:105 (July) 1933.

tion. Chart 1 compares the 2,000 readings reported in 1933 with the 1,100 made during the past year. The averages are practically identical for the ages from 3 to 32 weeks. The readings for the ages from 32 to 80 weeks were approximately 0.6 Gm. higher in this study than they were in the previous one. However, if the number of readings had been the same even this difference might have disappeared. The characteristic high value at birth, which falls rapidly and reaches its lowest level, about 11.7 Gm., at the ages from 8 to 12, is shown in both graphs. Because of deficient aeration of blood during intra-uterine life, the concentration of hemoglobin is high at birth. After birth, there is a marked change in oxygen tension. Mackay [15] stated that increased hemolysis, diminished red blood cell production and hydremia

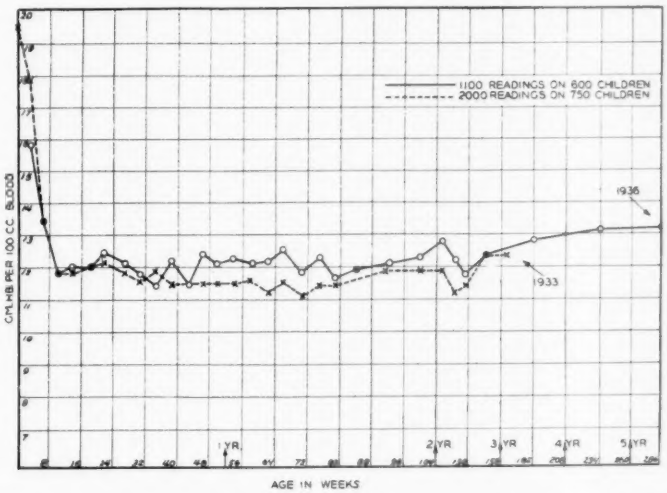


Chart 1.—A comparison of the hemoglobin curves obtained for normal infants in 1933 and in 1936.

may all play a part in bringing about the excessive fall. Abt [16] called attention to the fact that the fragile immature red blood cells and the embryonal type of hemoglobin differ both chemically and spectroscopically from the red blood cells and the hemoglobin of older infants.

Since the hemoglobin content and the erythrocyte count drop concurrently during the first weeks of life,[17] the cause would not be con-

15. Mackay, H. M. M.: Early Anemia of Premature Infants, Arch. Dis. Childhood **10**:195 (June) 1935.

16. Abt, A. F.: Anemia of Premature Infants, Am. J. Dis. Child. **49**:1204 (May) 1935.

17. Parsons, L. G.: Studies in Anemias of Infancy and Early Childhood, Arch. Dis. Childhood **8**:85 (April) 1933.

sidered one of iron deficiency. In chart 2, the curves for cases 1 and 2 show that this early drop in hemoglobin cannot be prevented by the administration of either iron or iron supplemented with copper. The success of the iron and copper therapy when extended indicates that the anemic condition of the later period is due to an iron and copper deficiency, while the low hemoglobin content at 13 weeks is related to an insufficiency of the hematopoietic system. If hemolysis in the new-born is severe and unchecked, profound anemia may result.

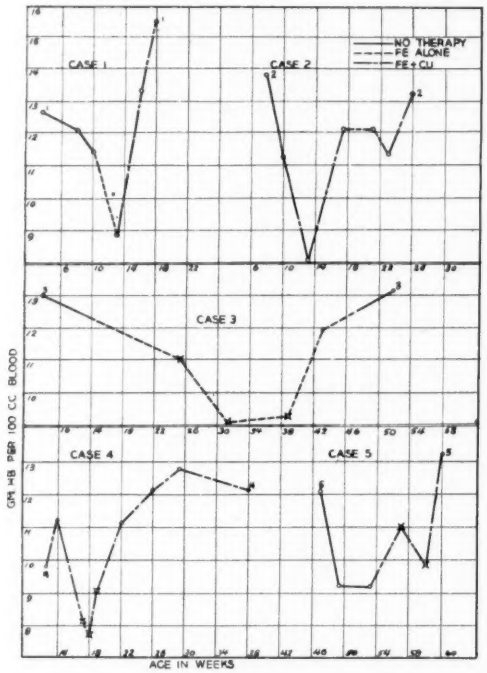


Chart 2.—Curves showing the ineffectiveness of therapy during the first few weeks of life (cases 1 and 2) and curves showing the interference by infection with the effect of treatment (cases 3, 4 and 5).

If the child is healthy and well fed and has a sufficient reserve of iron and copper to prevent an abnormally low drop in hemoglobin, the hemoglobin curve will be like that in chart 1, which shows that the average level during the first two years of life is approximately from 11.5 to 12.5 Gm. per hundred cubic centimeters of blood. From this time on there is a gradual increase. At 5 years, the average hemoglobin content is 13 Gm. This study included only preschool children, but other investigators have shown that the gradual rise continues until adolescence, when the adult level is reached.

Most authorities agree that infections interfere with the rate of regeneration of the blood. Cason,[13] Mackay,[18] Lewis[19] and others observed that the hemoglobin content not only tends to fall but also fails to respond to treatment until after the active infection has subsided. Gorter[3] reported that there is a higher level of copper in the blood of patients suffering from infectious diseases and anemia than in the blood of normal persons. He explained that there must be a mobilization of copper to fill the demand for an increased production of hemoglobin.

In cases 3, 4 and 5, illustrated in chart 2, the infant had nutritional anemia and was being observed at the clinic when an active infection interfered with the treatment being given. In case 3 the child showed no response to iron until after the infection had subsided. In cases 4 and 5 the patient responded to iron and copper therapy before and after the illness, but the therapy was ineffective during the infection. Certainly this is a problem worthy of further study. Robscheit-Robbins and Whipple[20] suggested that anemia follows infection because of a disturbance of internal body processes connected with food utilization. She stated that it is not due to lack of absorption of blood-forming substances or to destruction of blood.

While it is difficult to obtain a satisfactory hemoglobin response in anemic children who are suffering from a complication such as infection, the treatment of simple nutritional anemia has proved to be easy and to yield satisfactory results. One hundred and sixty preschool children were treated by the administration of iron alone or of iron supplemented with copper.

Chart 3 shows the typical hemoglobin response in 6 anemic infants to iron alone. In case 9 the hemoglobin rose from 11.2 Gm. per hundred cubic centimeters of blood to 12.1 Gm., but the higher value could not be maintained by therapy, and the hemoglobin fell again to an anemic level. In case 10 the level increased from 10.2 Gm. at the age of 36 weeks to 11.8 Gm. at 69 weeks. While this is an appreciable response, it is still below the average, and the level fell again within the next six weeks. In case 11 practically no response was shown. In case 8 there was one of the best increases in hemoglobin that we were able to obtain by treatment with iron alone, 3.5 Gm. When the admin-

18. Mackay, H. M. M.: Nutritional Anemia in Infancy with Special Reference to Iron Deficiency, Medical Research Council, Special Report Series, no. 157, London, His Majesty's Stationery Office, 1931.

19. Lewis, M. S.: Iron and Copper in Treatment of Anemia in Children, J. A. M. A. **96**:1135 (April 4) 1931.

20. Robscheit-Robbins, F. S., and Whipple, G. H.: Infection and Intoxication: Their Influence upon Hemoglobin Production in Experimental Anemia, J. Exper. Med. **63**:767, 1936.

istration of iron was discontinued, the hemoglobin level fell, and iron alone failed to bring it back to the high level previously obtained. In cases 6 and 7 there was no response to iron therapy.

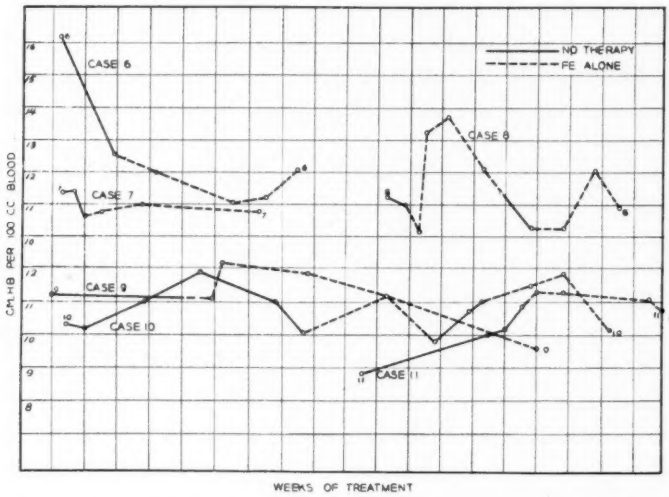


Chart 3.—Curves showing the hemoglobin response to the administration of 25 mg. of iron daily.

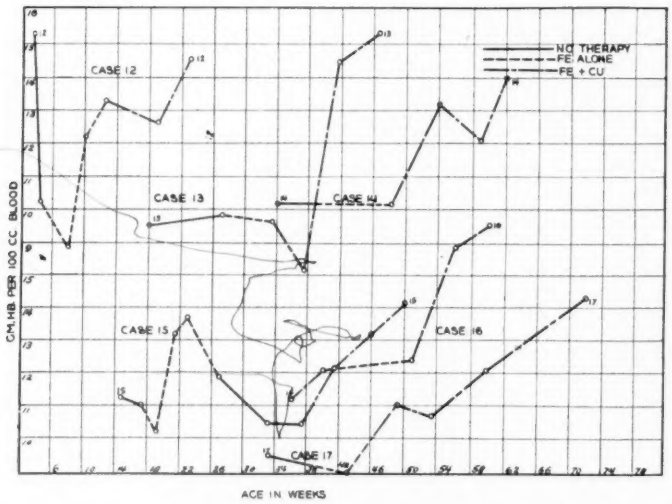


Chart 4.—Curves comparing the hemoglobin response to 25 mg. of iron plus 1 mg. of copper with that to 25 mg. of iron alone.

Seventy anemic infants and preschool children were treated with iron and copper, and satisfactory results were obtained. The addition of copper caused the hemoglobin content to rise more rapidly and to

reach a higher level. The curves for these children were similar to those reported last year.[1]

To compare the effectiveness of iron alone with that of iron fortified with copper in treating the same anemic infant, chart 4 is included. The response in these six cases was typical. While there was usually a slight rise in the hemoglobin content after the administration of iron alone, the maximum level was not obtained until supplemental copper was given. In case 15 the highest level reached when iron alone was given was 13.7 Gm. of hemoglobin per hundred cubic centimeters, and the level dropped back to 11.7 Gm. while the iron was still being administered. After administration of iron plus copper was started the hemoglobin content rose steadily to 14.1 Gm. In case 16 an increase from 10.4 to 11.5 Gm. was obtained by the administration of iron alone. The medication was changed to iron and copper, and the hemoglobin content rose rapidly to a level above the average. In case 17 no response to iron alone was shown, and there was an excellent response when supplemental copper was given. In cases 13 and 14 the picture was similarly impressive.

There is ample evidence to prove that iron alone is incapable of raising the hemoglobin content to the average level and that supplemental copper is necessary to stimulate an optimum response.

## CONCLUSIONS

1. If infants are healthy and well fed and have a sufficient reserve of iron and copper, an average level of from 11.5 to 12.5 Gm. of hemoglobin per hundred cubic centimeters of blood is maintained throughout the first two years of life. The average level is somewhat lower than the optimum level, from 12.5 to 13.5 Gm. After the age of 2 years there is a gradual increase, which continues until the adult level is reached, at adolescence.

2. Infection interferes seriously with the rate of regeneration of blood, and the administration of medicinal iron and copper is ineffective until after the active infection subsides.

3. Iron alone usually stimulates a slight increase in the formation of hemoglobin when given to anemic infants, but the response is inadequate; the hemoglobin content does not reach the average level for healthy infants.

4. Iron supplemented with copper causes a maximum response in the regeneration of hemoglobin when administered to anemic infants.

Lorna Willis, Elizabeth Whittle, Eleanor Wagner, Jane Strohn, Ann Kraft, and Bonnie Beilfuss assisted in this study.

# Case Reports

## DEATH DURING BLOOD TRANSFUSION AS A RESULT OF INTRACRANIAL HEMORRHAGE

### CASE OF AN EIGHT DAY OLD INFANT

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AND
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Death from cerebral hemorrhage occurring a week or more after birth and due to an injury presumably sustained at birth is rare in infants who show no signs of cerebral hemorrhage at birth and who develop normally until death. Two such cases in the literature were reviewed in 1929 by Glaser,[1] who added a third of his own. Since then, so far as we have been able to determine, no other cases of this nature have been reported. The one described, because of the rarity of the occurrence, and because of the lessons which may perhaps be drawn from it, is considered worthy of reporting in an attempt to add to the knowledge of this fortunately uncommon condition.

The infant was first seen by the pediatric consultants at the age of 8 days. A ritual circumcision had been performed by an experienced mohel about six hours previously. Shortly afterward the infant started bleeding profusely and steadily from the site of the operation. Local measures, as well as the intramuscular injection of some of the mother's blood, proved ineffective in controlling the bleeding. Transfusion was deemed necessary as a life-saving measure. Both mother and child belonged to group 3 (Moss), and cross-matching by two physicians working independently showed the bloods to be compatible. The infant's red corpuscle count was 3,770,000 and his hemoglobin content 70 per cent Sahli.

Transfusion was started through a vein in the scalp, the blood being given through a syringe 4 cc. at a time and very slowly because of the small size of the vein and of the needle used. In thirty-five minutes 54 cc. of blood and 20 cc. of physiologic solution of sodium chloride were given. There was the usual amount of struggling on the part of the child, but the procedure was going smoothly when he suddenly became cyanotic. Transfusion was immediately discontinued. Respirations ceased, and occasional cardiac sounds were heard only a moment or

From the departments of pediatrics and obstetrics of the University of Rochester School of Medicine and Dentistry and the department of obstetrics of the Rochester General Hospital.

1. Glaser, J.: Late Death as a Result of Cerebral Hemorrhage at Birth, Am. J. Dis. Child. **37**:807 (April) 1929.

two longer. Artificial respiration, with carbon dioxide and oxygen, the subcutaneous administration of caffeine with sodium benzoate and the intracardiac administration of epinephrine were ineffective.

In attempting to explain the cause of this infant's death, we considered the following explanations as being most probable: (1) intracranial hemorrhage at birth, with incomplete clot repair and loosening of this clot due to the disturbance in intracranial dynamics resulting from exsanguination and transfusion, (2) acute cardiac dilatation and (3) a congenital anomaly, possibly cardiac. Consideration of the infant's history made us regard the first explanation as the most probable. The patient was born at a full term, weighing 3,220 Gm. (7¼ pounds). The labor had been complicated by a deep transverse arrest. A Barton forceps was applied with moderate traction, and the head came down easily but did not rotate until nearly fully crowned. The second stage lasted about two and a quarter hours. The infant was of normal appearance, but there was difficulty in establishing extra-uterine respiration. The upper part of the respiratory tract was cleared of mucus by a suction pipet, and mouth to mouth insufflation was practiced. Inhalations of carbon dioxide and oxygen were administered, and 0.0016 Gm. of alphalobeline (1/40 grain) was given hypodermically. The child responded well, had no cyanotic attacks and developed into a vigorous infant who weighed 3,220 Gm. (7¼ pounds) at the time of death. He was breast fed. Slight jaundice, which was considered physiologic icterus neonatorum, appeared on the fifth day. The subsequent course of events has been described.

Necropsy was performed by Dr. I. Gaspar. A spinal puncture performed just previously yielded a profuse amount of bloody fluid. Marked anemia of all organs was present. The heart was of normal size, was contracted in systole and presented no abnormality except the puncture due to the injection of epinephrine. A cephalohematoma was present. When the skull cap was reflected, the supratentorial area appeared normal except for slightly bloody cerebrospinal fluid. The subtentorial area was filled with blood, and there was blood in the spinal canal. The source of the subtentorial hemorrhage could not be ascertained.

The intracranial hemorrhage was considered the cause of death. We feel that the most probable cause of the hemorrhage was that previously mentioned, namely, an injury to a blood vessel at birth, with incomplete clot repair, which made the vessel unable to withstand the dynamic changes secondary to the exsanguination and transfusion. However, since the site of such an injury was not discovered, we cannot absolutely rule out other possibilities.

The continuous oozing from the site of the circumcision wound and the extensive oozing into the skin at the sites of the intramuscular injections of blood speak in favor of some type of blood dyscrasia, though no familial condition of this nature is known. The mother's

Wassermann reaction of the blood was negative, and histologic examination of the child's tissues showed no abnormality except anemia. The late onset suggests some condition other than the so-called hemorrhagic disease of the new-born, which usually has its onset much earlier. True hemophilia is usually a familial disease and does not ordinarily appear as early as this. The condition in our case can hardly be classified as "temporary hemophilia," as described by Siedentopf,[2] because the bleeding occurred earlier in his case and there was no jaundice. However, because the circumcision wound resisted all the usually successful measures employed to secure hemostasis, we feel that blood dyscrasia cannot be ruled out, although we are at a loss to explain its nature.

Sepsis must be considered in every case in which bleeding and jaundice occur late, as they did in this instance. While we cannot absolutely rule out this condition, we think it an unlikely explanation because of the infant's normal development up to the time of circumcision.

The intracranial hemorrhage probably started either shortly after the beginning of the transfusion or near its end. There is no evidence that the hemorrhage could have started earlier. On the contrary, as Glaser [3] has pointed out in a study of intracranial hemorrhage in premature infants, a slowly bleeding subtentorial circum-medullary hemorrhage usually results in periods of intermittent cyanosis which are almost pathognomonic. In our case there was but one terminal attack of cyanosis, which would be evidence of a rather sudden hemorrhage. It does not seem probable that the large quantity of blood found in the subtentorial cerebrospinal space could have been poured out in the short interval between the terminal cyanotic attack and the patient's death, though one cannot be absolutely sure that it was not. It is possible that the prolonged efforts of artificial respiration forced significant quantities of blood out of the venous reservoirs of the chest and abdomen, back through the incompetent valves of the jugular veins, into the cerebral venous sinuses and thence into the subtentorial space.

All things considered, we believe the conclusion justified that death occurred as a result of intracranial hemorrhage due to an injury to a blood vessel sustained at birth in an unavoidably abnormal labor, plus blood dyscrasia of an unknown type. Nature apparently controlled the situation until the intracranial dynamics were disturbed by the hemorrhage from the circumcision wound and the transfusion following it. If this assumption is correct, the lesson to be learned, which has not previously been stated in pediatric literature so far as we can discover, is that in cases in which there is a history of difficult labor, regardless

2. Siedentopf, E.: Temporäre Hämophilie der Neugeborenen, Centralbl. f. Gynäk. **53**:1068, 1929.

3. Glaser, J.: Cerebrospinal Fluid of Premature Infants, Am. J. Dis. Child. **40**:741 (Oct.) 1930.

of whether or not there have been signs of cerebral hemorrhage at birth, elective operations, such as circumcision, should be deferred until all danger of incompletely organized intracranial clots is past, that is, for at least one or two months. If this is impracticable, careful studies of the bleeding time and the coagulation time should be made. Furthermore, if operation is necessary and transfusion must subsequently be carried out, it is better to give the blood in small, frequently repeated transfusions than to give it in the customary single, large transfusion. While we ordinarily hesitate to draw conclusions from one case report, we feel justified in doing so in this case because the precautions to be observed are so simple and they may avert a tragedy such as we experienced.

# WEBBED NECK (PTERYGIUM COLLI)

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CHICAGO

The congenital formation of a web of skin extending from the mastoid area to the region of the acromion process is unusual, especially when found without developmental anomalies of the cervical portion of the spine.

In 1883 Kobylinski [1] described webbing of the skin on the lateral aspects of the neck and suggested its possible relation to congenital short neck. In 1902 Funke [2] described this condition in a 15 year old girl, using the term pterygium colli. In his case there were associated abnormalities of the breast and nipples and absence of pubic and axillary hair. Bussière [3] in 1902 reported webbing of the neck in a Hindu boy 12 years of age. In 1912 Klippel and Feil [4] reported a case in which webbing of the neck was associated with congenital malformation of the cervical part of the spine. Drachter [5] in 1923 reported a case in which webbed neck ("dove neck") was found with osteomyelitis. The presence of suboccipital encephalocele in this case suggests a diagnosis of the Klippel-Feil syndrome rather than of webbed neck. Frawley [6] in 1925 reported webbing of the skin of the neck in sisters 12 and 16, another case in a woman of 28 and one in a girl of 7 years. Roentgenograms of the cervical part of the spine were normal. In the last case there was associated webbing of the axillary

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From the department of orthopedic surgery of the Children's Memorial Hospital.

1. Kobylinski, O.: Ueber eine flughautähnliche Ausbreitung am Halse, Arch. f. Anthrop. **14**:343-348, 1883.

2. Funke: Pterygium Colli, Deutsche Ztschr. f. Chir. **63**:162-167, 1902.

3. Bussière, J. A.: L'homme au cou de capelle, dévelopement anormal d'un faisceau musculaire acromio-mastoïdien rudimentaire, malformation congénitale rare, observée à Pondichéry (Indes Orientales), Ann. d'hyg. et de méd., Colon **5**:686-688, 1902.

4. Klippel, M., and Feil, André: Un cas d'absence de vertèbres cervicales avec cage thoracique remontant jusqu' à la base du crâne (cage thoracique cervicale), Nouv. iconog. de la Salpêtrière **25**:223-250, 1912.

5. Drachter, R.: Demonstration, Klin. Wchnschr. **2**:664, 1923.

6. Frawley, John M.: Congenital Webbing, Am. J. Dis. Child. **29**:799-805 (June) 1925.

folds. In 1928 DeBruin [7] reported a case in a girl 6 weeks of age. There was extreme shortness of the skin in a vertical direction on both sides of the neck. Roentgenograms of the cervical part of the spine revealed nothing abnormal. Sections of the folds of the neck obtained at autopsy revealed muscle and suggested an abnormal distribution of the platysma myoides. The deep fascia and muscles were not involved. Nageotte-Wilbouchevitch [8] in 1934 reported three cases in women. In two the condition suggested some endocrine dysfunction because of associated dwarfism.

Webbed neck, or pterygium colli, should be differentiated from the large group of conditions in which pseudo webbing is present as a part of the general picture of maldevelopment of the cervical area and especially of the cervical part of the spine. In the latter conditions the low hair line and the increased width of the neck reflect the skeletal deformity rather than an abnormality of the skin alone. In Sprengel's deformity, the high position of the scapulae and the presence of omovertebral bones result in apparent lowering of the hair line and may suggest webbing of the skin. The skin, however, is normally pliable and fits snugly over the malformed deeper structures.

In typical webbing of the neck, the cervical part of the spine, the muscles and the fasciae are normal. The skin of the lateral aspects of the neck lies in long, sweeping folds that extend from the mastoid and postauricular areas to the region of the acromion processes. The apex of the cutaneous fold is inelastic in the vertical direction, restricting lateral bending of the cervical part of the spine by its tension on the lateral aspects of the shoulder girdle. The shoulders are held moderately high. Because of this tension, movement of the cervical portion of the spine is reduced, and the patient turns the entire trunk to the right or left instead of the head alone. The hair line is low, and the skin over the back of the neck is loose and freely movable on the deep fascia. Folds may be grasped by the hand, giving the impression of a great excess of skin over this area. The surfaces of the web itself may be rolled between the fingers, giving the impression of tightness within the skin rather than in the deeper structures. The upper part of the auricle is bound to the margin of the scalp by skin which bridges the normal angle behind the triangular fossa. The concha is inverted, projecting laterally and anteriorly so as nearly to obliterate the external meatus. A pterygium overlying the inner canthus of the eye may be present. The skin forming the axillary, antecubital

7. DeBruin, M.: Pterygium Colli Congenitum, Am. J. Dis. Child. **36**:333-341 (Aug.) 1928.

8. Nageotte and Wilbouchevitch: Bull. Soc. de pédiat. de Paris **32**:683-688 (Dec.) 1934.

and inguinal folds and creases is more rounded and smoother than usual. Abnormal development of the breasts has been described.

The etiology of the web formation is not clear, since the cutaneous fold is unrelated to the structural changes of the cervical part of the spine and the muscles. The normal occurrence of pterygium colli in the chimpanzee suggests the possibility that the webbing in man is a manifestation of atavism (Nageotte-Wilbouchevitch). In all probability there is an inherent defect in the skin itself.

Correction of webbed neck is indicated, first, because of its restriction of the normal range of motion of the head and shoulder girdle and, second, for cosmetic reasons. The excess of skin in the horizontal plane, combined with tightness in the vertical plane, permits the use of plastic procedures, especially those of the Z skin plasty type.

## OPERATION

A vertical incision 1½ inches (3.8 cm.) long (fig. 1, *B-C*) is made along the central portion of the crest of the skin fold, just anterior to the lateral part of the hair line. A horizontal incision (fig. 1, *I*) extending anteriorly at right

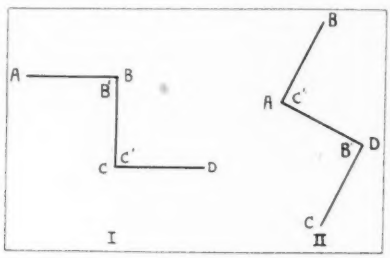


Fig. 1.—Diagram of the incision (*I*) and the closure (*II*).

angles 1½ inches (3.8 cm.) (fig. 1, *A-B*) and a similar incision extending posteriorly (fig. 1, *C-D*) are made. The skin and subcutaneous tissues are freed from the deep fascia. Closure is obtained by reversing the relative positions of the angular flaps *B* and *C*, as shown in figure 1, *II*. This method permits a lengthening of 1⅞ inches (4.8 cm.) in the vertical direction and a shortening of about 1⅝ inches (about 4.1 cm.) in the horizontal direction. A firm, bulky pressure dressing is applied, which holds the head flexed to the opposite side.

## REPORT OF CASES

CASE 1.—T. P. was a white boy aged 9 years whose chief complaint was deformity of the neck. Birth had been difficult. He was the fifth child. He had had an acute infection of the respiratory tract two years ago. The family history contained nothing relevant. The patient was a well nourished boy in good general health. Examination revealed nothing abnormal except the deformity of the neck and ears. The neck appeared short and wide and had an unusually low hair line. Loose folds of skin extended from the mastoid area to the base of the acromion processes. These folds became tense on lateral flexion of the cervical part of the spine, causing restriction of all movements. The folds of

skin were loose in the horizontal plane but inelastic vertically. The cutaneous folds of the joints of the upper and lower extremities were normal. The upper portion of the conchae of both ears was fixed closely to the scalp by skin which appeared to be an extension of the cervical webbing (fig. 2). Roentgenograms of the cervical part of the spine showed no vertebral anomaly.

On June 25, 1934, an operation on the right side of the neck was performed. The cutaneous fold and subcutaneous tissue were divided transversely for 2 inches (5 cm.). The underlying muscle and fasciae were normal. The incision was closed vertically. Healing was uneventful, under pressure dressings. The result was satisfactory.

On Aug. 28, 1934, an operation on the left side of the neck was performed. The fold of skin was divided transversely, and the defect was filled with a

Fig. 2 (case 1).—T. P. before and after operation.

free, full thickness graft from the abdomen. Some superficial necrosis of the graft occurred. Healing otherwise was satisfactory, although the scar was more noticeable than was desired.

CASE 2.—G. C. was a white boy aged 9 years. Delivery had been instrumental. He appeared to be normal physically except for deformity of the neck and ears and abnormal distribution of skin flaps, in the form of pterygiums, over the inner canthi of the eyes. The upper portion of the ears was held close to the upper mastoid area by folds of skin. The external auditory meatus was occluded by inversion of the concha. Folds of skin extended from the mastoid areas to the region of the acromion process. These folds appeared to be detached from the deeper structures and suggested excessive length in the horizontal plane. The hair line was low, giving the neck an appearance of being short. The anterior axillary folds were smooth and slightly more prominent than usual. The sides of the neck showed symmetrical deformity (figs. 3 and 4). Roentgenograms of the cervical part of the spine showed normal vertebrae.

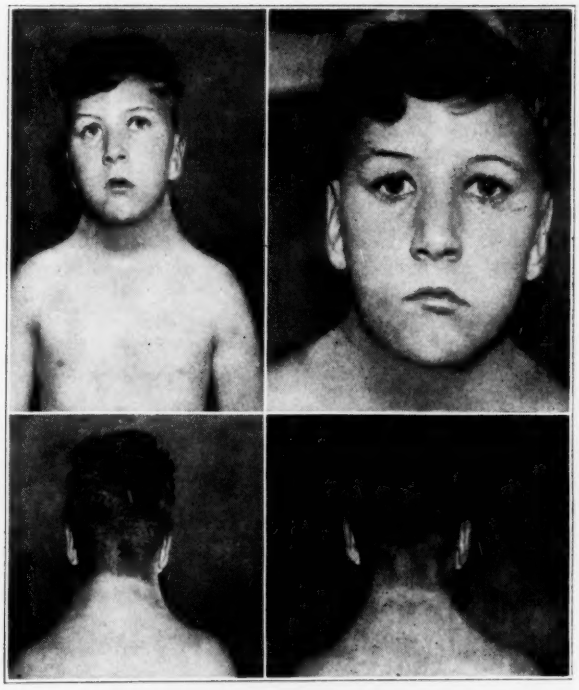

Fig. 3 (case 2).—G. C. before and after operation.

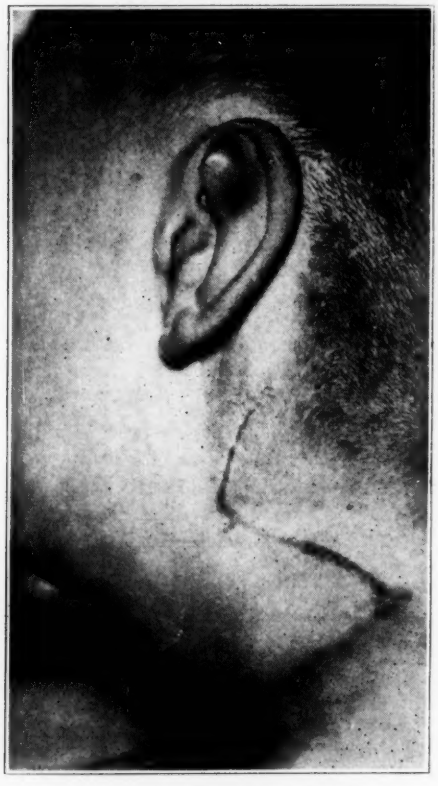

Fig. 4 (case 2).—The operative scar. The external auditory meatus may be noted.

On Sept. 3, 1935, an operation was performed on the left side. A "Z" type incision was made over the apex of the cutaneous fold on the left, extending through the subcutaneous tissue to the superficial cervical fasciae (fig. 1, *I* and *II*). The skin was found to be freely movable on the superficial fascia. No fibrous or muscle tissue was found in the skin flaps. Closure was carried out as indicated in figure 1, *II*, and a heavy, bulky compression dressing was applied. Sutures were removed on the eighth day, and the wound showed good healing.

On Sept. 17 a similar operation was performed on the right side.

# MENINGITIS COMPLICATING MUMPS AND ENCEPHALITIS COMPLICATING MEASLES IN THE SAME CHILD

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## MENINGITIS COMPLICATING MUMPS

J. P., a Greek boy aged 6 years, was first admitted to the Doernbecher Memorial Hospital for Children on Nov. 17, 1934. Six days previously he had complained of soreness around his gums and lips on the right side and had had trouble with eating because of pain in the jaw. He was seen two days later, five days before admittance to the hospital, at which time a large swelling over the region of the parotid gland was noted. Both orifices of Stensen's duct were inflamed, and a diagnosis of mumps was made. For the next five days, until he entered the hospital, he continued to have fever, his temperature going up to 104 F., and his appetite was poor. He became irritable and thrashed wildly about on his bed. A few days before entrance to the hospital he complained of extreme pain in his legs, especially about the knees. The neck became rigid and the Kernig sign positive. When the child was admitted to the hospital no other essential findings outside of cryptorchidism were noted. A spinal puncture revealed clear fluid; the pressure was not noted. The cell count was 119. The Kolmer and the Kahn reaction were negative.

For two days the boy's temperature was between 103 and 104; it became normal on the third day. The rigidity of the neck gradually decreased, and the irritability gradually left. On November 19, two days after the boy's entrance into the hospital and nine days after his illness began, he was discharged. A week later he was examined, and no evidence of any disease was noted.

## ENCEPHALITIS COMPLICATING MEASLES

On Feb. 9, 1936, this child was seen with measles during an epidemic. He was broken out completely, and during the next few days his convalescence was uneventful. Five days after his initial rash he began to get irrational, and during the next few days he became delirious and thrashed about on the bed. His temperature ranged near 104 F. Occasionally he relaxed, and then the breathing was irregular, with apneic pauses of various lengths. The respirations after these pauses were of irregular length and depth.

The child reentered the hospital, where a spinal puncture revealed normal spinal fluid. The temperature was 102 F. and gradually subsided, reaching normal by the sixth day in the hospital. The only therapy was the administration of fluids subcutaneously because of the child's inability to take fluids. On about the fifth day in the hospital he became more rational and was able to care for himself in a normal manner. He was discharged, and an examination three weeks later revealed that he was free from sequelae.

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## COMMENT

A case of meningitis complicating mumps and encephalitis complicating measles in the same child is presented. The question is raised as to why one should react to different virus diseases with the complication of two similar diseases. The fact that these two similar conditions did occur should be brought to the attention of physicians, since it may explain similar occurrences and help physicians in their conclusions.

# Progress in Pediatrics

## VAGINITIS OF CHILDREN

### A REVIEW OF THE LITERATURE

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At present there is a vigorous campaign throughout the world against venereal disease. Although the attention of both the medical profession and the laity is being spurred by militant publicity, the problem of gonorrhea in the child remains almost completely neglected. The presence of this disease is rarely suspected, and the ignorance of both the lay public and the medical profession is the greatest obstacle to urgently needed concerted action for the control, study and prosecution of obviously required public health measures. Further, most of the recent articles in the literature are concerned with the treatment of the disease but totally disregard the larger problem of the social aspects, the public health question and the psychologic effects of the disease on the child. The few articles which call attention to these problems appear at irregular intervals and leave no deep or permanent impression on the medical profession, the social service agencies or public health officials. One finds, widespread, a dread of the appearance of the disease and the formulation of methods preventing the entrance of infected children into hospitals, nurseries, orphanages and convalescent homes. The exclusion of these children from schools removes them from restraint and training and leaves them marked among their playmates. Is it unexpected that such children become problem children, juvenile delinquents and maladjusted adults? Is it surprising that they feel themselves to be and are treated as the outcasts, the pariahs, of society?

Add to this the reaction of the relatives of these children, who in the majority of cases belong to the poorer classes. If they place any importance at all on the presence of a vaginal discharge, they associate it with venereal disease and cannot help making the child aware of the stigma attached to it. The irony of the situation lies in the fact that in the great majority of cases this is not a venereal disease in the true meaning of the word but is contracted innocently.

From the Department of Pediatrics, Metropolitan Hospital.

Further, the complications which occur present a hazard to the future health and happiness of the affected person. If there is a possibility that sterility or ectopic pregnancies may occur as sequelae of the disease, certainly the medical profession must actively fight the infection with all the energy used in combating gonococcic infections in adults.

The disease is of great importance to the community as well as to the individual. Besides clearing up the social and educational problems raised, the community must provide methods for the control and prevention of the disease. Besides solving the problems of isolation and prevention, hospitals and other institutions must provide adequate facilities for treating other acute and chronic ailments in children suffering from vaginitis and for giving institutional care to these children as it becomes necessary. In New York the clinical problem lies in the inadequacy of the facilities available. In some dispensaries children with vaginitis are treated in the gynecology clinic. No separate records are kept, and no one can tell what children or how many are attending the clinic, how often they come for treatment or whether they come at all, whether the smears made are positive when examined for gonococci or any other pertinent fact.

This lack of interest is easily explained by the disappointing results obtained in treating the disease, its chronicity and the general impression that spontaneous cure occurs at puberty and that the disease is of little importance to the child. If concerted and honest attempts were made, a solution could be found for the following fundamental problems which must be solved before any success can be achieved in treating the disease.

1. Actual incidence
2. Sources of infection
3. Age limits
4. Period of contagiousness
5. Causative agent
6. Pathologic factors
7. Complications
8. Relation of ophthalmia to vaginitis
9. Incidence of proctitis and urethritis and their relation to recurrence
10. Recurrence
11. Latency and carriers
12. Adulthood and sequelae
13. Criteria of cure
14. Methods of prophylaxis and control
15. Exclusion of infected children from school and the social and the psychologic aspects

## REVIEW OF THE LITERATURE

The literature on gonococcic vaginitis is moderately large and is generally distinguished by three features: the disagreement on many basic facts, the great variety of therapeutic methods and the lack of statistics. Reviews of the literature were published in 1908,[1] 1912,[2] 1917[3] and 1926.[4]

## ACTUAL INCIDENCE

Dooley[5] recorded 300 new cases in one year (1927) in Baltimore, while Hamilton[6] reported that during a twenty year period 5,000 patients had been treated at the Vanderbilt Clinic in New York. Wehrbein[7] attempted a survey of the incidence of the disease in the city of New York but could obtain no reliable data. She concluded that the ailment occurred with sufficient frequency to be a definite problem in the field of child health. Oppenheimer and Everett[8] attempted a similar survey in Washington, D. C., and found the same conditions existing there. Brunet and Dickenson[9] estimated that from 1 to 5 per cent of young females in the poorer sections of cities had the infection. McElroy[10] wrote that the disease was much more frequent than was suspected and cited Pollack's estimate of from 800 to 1,000 new cases occurring each year in Baltimore. Von Zumbusch[11] reported cases occurring in rural communities. Nelson[12] published the reported incidence in Massachusetts. In the period from 1919 to 1925 there were 494 cases, comprising 9 per cent of the total cases of gonorrhea in females, and in the period from 1925 to 1928 there were 648 cases,

1. Hamilton, A.: J. Infect. Dis. **5**:133 (March) 1908.

2. Genersich, G.: (*a*) Pest. med.-chir. Presse **47**:405 (Dec. 17) 1911; (*b*) **48**:9 (Jan. 7) 1912.

3. Gittings, J. C., and Mitchell, A. G.: Review of the Literature of the Past Five Years on Gonococcus Vulvovaginitis in Childhood, Am. J. Dis. Child. **13**: 438 (May) 1917.

4. Fraser, A. R.: Ven. Dis. Inform. **7**:1 (Jan.) 1926.

5. Dooley, P.: Gonorrheal Vulvovaginitis: Possible Sequelae in Adult Life, Am. J. Dis. Child. **42**:1086 (Nov.) 1931.

6. Hamilton, B. W.: Ven. Dis. Inform. **8**:84 (March) 1927.

7. Wehrbein, K.: Arch. Pediat. **44**:243 (April) 1927.

8. Oppenheimer, E., and Everett, R. H.: J. Social Hyg. **20**:129 (March) 1934.

9. Brunet, W. M., and Dickenson, R. L.: Ven. Dis. Inform. **10**:1 (April) 1929.

10. McElroy, A. S.: Pennsylvania M. J. **34**:192 (Dec.) 1930.

11. von Zumbusch, L.: Deutsche med. Wchnschr. **57**:421 (March 6) 1931.

12. Nelson, N. A.: New England J. Med. **207**:135 (July 21) 1932.

or 11 per cent of the total. In England Brown [13] collected reports of 118 cases in five years, comprising 12.5 per cent of the total cases of gonorrhea in females reported. Dobszay [14] in 1933 said that in Germany, after the great economic and sociologic changes which had taken place, there was a significant rise in the morbidity of this disease. Notes [15] reported 120 new cases in one year in Washington, D. C. In answer to the Children's Welfare Federation's questionnaire,[16] 59 clinics in New York City reported registration of 1,013 cases of gonorrheal vaginitis in 1933.

At our clinic, started twenty-one months ago, we have had over 300 patients registered, and for the last six months we have averaged about 20 new patients each month. Although they come from the entire city, a great majority come from a single area comprising the poor section served by the Metropolitan Hospital and the Harlem Hospital.

Some authors [4] have stated the opinion that most children with vaginal discharge are suffering from gonorrheal vaginitis. These authors have said that when the organisms cannot be found it is due to secondary invaders. They have suggested that gonococci would prove to be present in all such patients if smears were made in the early stages of the disease. On the other hand, Stein and his co-workers [17] found gonococci in only 21 per cent of their patients. Ruys,[18] who employed cultures as well as smears, obtained positive results only in patients with acute attacks and considered all others to have a nonspecific infection. She concluded that gonorrheal vaginitis occurs only in the acute form and warned against making a diagnosis of this condition too frequently. We shall not discuss further the comparative incidence of specific and nonspecific vaginitis but shall consider only gonorrheal vaginitis.

## SOURCE OF INFECTION

The consensus seems to be that adults are the most frequent source of infection and that children are infected innocently. Hospitals and

13. Brown, D. K.: Brit. J. Ven. Dis. **6**:285 (Oct.) 1930.

14. Dobszay, L.: Arch. f. Kinderh. **99**:102 (April) 1933.

15. Notes, B.: Arch. Pediat. **47**:58 (Jan.) 1930.

16. Tentative Standards for Vaginitis Clinics, Children's Welfare Federation, New York City, 1936.

17. Stein, I. F.; Leventhal, M. L., and Sered, H.: Cervicovaginitis: A Study of Two Hundred and Ninety-Six Consecutive Cases, Am. J. Dis. Child. **37**:1203 (June) 1929.

18. Ruys, A. C.: The Etiology of Vulvovaginitis Infantum, J. A. M. A. **105**:862 (Sept. 14) 1935.

other institutions are blamed in many cases. Playmates and articles such as toilet seats, linen and thermometers [19] also are implicated. Rape and assault are believed to play but a small part in spreading the disease,[20] although Paine [21] and McKelvey and his colleagues [22] expressed the opinion that venery is an important factor. Fraser [4] reported that the hands of colored maids and the toilet seat accounted for 90 per cent of his cases. Vogt [23] and Epstein [24] stated it as their belief that infection takes place during delivery but remains latent. Norris and Mickelberg,[25] on the other hand, stated that infection at birth is rare. Risch [26] summarized the literature on vaginitis in the new-born and could not determine whether the infection occurred during delivery or afterward. Thomas and Bayne-Jones quoted Slobozianu and Herscovici, who described three instances in which the patient was born with the disease.[27] They concluded that in 2 of the patients the only possible portal of entry was the placenta.

Most of the statistics in the literature were obtained by questioning the parents. Sometimes it was possible to check the accuracy of the replies by investigating hospital records, the presence of gonorrhea in various members of the family and other factors. It was, however, manifestly impossible to do this when such things as toilet seats, linen and bathing water were accused. Thus Brunet and Tolle examined members of the families of 113 patients and found evidence of gonorrhea in 92 per cent of them.[28] Dobszay,[14] feeling that infected objects are an important source of infection, took cultures at frequent intervals from various materials which were contaminated either artificially or

19. Hamilton.[6] Brunet and Dickenson.[9] Dobszay.[14] Stein, Leventhal and Sered.[17]

20. (*a*) Genersich.[2a] (*b*) Hamilton.[6] (*c*) Dobszay.[14] (*d*) Stein, Leventhal and Sered.[17] (*e*) Pisacane, C.: Studium **17**:142 (April 20) 1927. (*f*) Fessler, A.: Urol. & Cutan. Rev. **34**:444 (July) 1930. (*g*) Genersich, G.: Pest. med.-chir. Presse **48**:2 (Jan. 1) 1912.

21. Paine, A. K.: New England J. Med. **207**:137 (July 21) 1932.

22. McKelvey, S. R., and others: Ven. Dis. Inform. **6**:289 (Oct.) 1925.

23. Vogt, E.: Ven. Dis. Inform. **8**:97 (March) 1927.

24. Epstein, B.: Jahrb. f. Kinderh. **139**:23, 1933.

25. Norris, C. C., and Mickelberg, H. B.: Arch. Pediat. **39**:281 (May) 1922.

26. Risch, P.: Zur Kenntnis der Vulvovaginitis gonorrhoica bei Neugeborenen, Jena, G. Neuenhahn, 1926.

27. Thomas, R. B., and Bayne-Jones, S.: Am. J. Syph., Gonor. & Ven. Dis. (supp.) **20**:99 (Jan.) 1936.

28. Brunet, W. M.; Tolle, D. M.; Scudder, S. A., and Medcalf, A. R.: Cervico-Vaginitis of Gonococcal Origin in Children, Hosp. Social Service Mag., supp. 1, March 1933.

by letting infected children play with them. He found that positive cultures were obtained for various lengths of time, as follows:

| | |
|---|---|
| Rabbit skin | 54 hours |
| Dry linen | 12 hours |
| Wet linen | 24 hours |
| Wood | 2 hours |
| Metal | ½ hour |
| Rubber | 2 hours |
| Water | 2 hours |
| Soapy water | less than 10 minutes |
| Urine | 12 hours |
| Stool | 36 hours |

The following tabulation is a summary of statistics on the sources of infection, as stated by various authors:

| | |
|---|---|
| Unknown | 367 |
| Family (including other children, etc.) | 444 |
| Clothing (diapers, etc.) | 135 |
| Hospitals and other institutions | 46 |
| Playmates | 49 |
| Nurses | 28 |
| Assault | 14 |
| Sexual delinquency | 11 |
| Direct transmission | 8 |
| Public schools | 8 |
| Total | 1,110 |

At our clinic 195 parents named the following sources:

| | |
|---|---|
| Unknown | 95 |
| Hospitals and other institutions | 71 |
| Family | 26 |
| School | 3 |

They claimed that 27 of these patients acquired the infection at the Metropolitan Hospital. The records were available and on investigation yielded the following information:

| | |
|---|---|
| Probably infected at the hospital | 5 |
| Possibly infected at the hospital | 6 |
| Definitely not infected at the hospital | 14 |
| No record of a stay in hospital | 2 |

A large but unknown percentage of the mothers of these children have been operated on for various pelvic conditions.

### AGE LIMITS

Gonorrheal vaginitis of children can occur at any age from birth until puberty. However, in the literature there are few instances of proved infection at birth or within the first few days after birth.[26] In

the majority of such instances, although not in all, gonorrheal vaginitis is preceded by gonorrheal ophthalmia neonatorum. In one of our cases the first smear was taken on the eleventh day and was positive. In the majority of the cases reported positive smears usually cannot be obtained until about the third week of the patient's life. In the light of the newer knowledge of endocrinology, Allen and Diddle [29] pointed out a possible explanation for this. During pregnancy there is a notable rise in the estrogen content of the maternal tissues and body fluids. Tests for estrogen in the umbilicus and in the blood of the new-born child have been found to give positive results. Further, it has been pointed out that the amount of estrogen in the infant rapidly decreases after birth. It is possible, then, that the new-born infant is protected from contracting vaginitis by an estrogenic reaction similar to that of the adult vaginal epithelium. This protection would be of short duration. There is evidence that this might be so in the work of Wynkoop and Pennock,[30] who took smears from 1,150 female infants on the first, fourth and thirteenth days. Although in 19 (1.6 per cent) there developed gonorrheal ophthalmia, none showed gonorrheal vaginitis. It is interesting to note that in 60 per cent of these infants a discharge developed at some time during the period but that in no case were gonococci present, the discharge consisting mainly of leukocytes. Wynkoop and Pennock found that 17 per cent of the children had a discharge on the first day, 21 per cent on the fourth day and 43 per cent on the thirteenth day. Notes and Neuman [31] took intravaginal smears from 500 female infants at the time of their delivery and at the time of their discharge from the hospital (about the tenth day). Three cases were regarded as instances of gonorrheal vaginitis in the new-born, but the earliest positive smear was found on the nineteenth day, and 2 of the 3 infants had ophthalmia neonatorum. Rorke [32] described a case of vaginitis following breech delivery in which ophthalmia did not develop. The discharge began a few days after birth, and positive smears were obtained on the fourteenth day. Positive smears were obtained from the mother also.

As to the other age limit, it is the general impression that the disease undergoes spontaneous cure at puberty. Wrana [33] disagreed with this, basing his opinion on the fact that the organisms may remain in the deep tissues without there being any superficial reaction. He stated

29. Allen, E., and Diddle, A. W.: Am. J. Obst. & Gynec. **29**:83 (Jan.) 1935.

30. Wynkoop, E. J., and Pennock, W.: New York State J. Med. **32**:1192 (Oct. 15) 1932.

31. Notes, B., and Neuman, H.: M. Ann. District of Columbia **3**:306 (Dec.) 1930.

32. Rorke, M.: Brit. M. J. **1**:671 (May 15) 1920.

33. Wrana, J.: Arch. Pediat. **52**:335 (May) 1935.

that it is then possible to have a recurrence of the infection just before puberty which would persist. Attending our clinic at present are 2 girls who have been menstruating for six and eight months, respectively, and whose vaginal smears still show gram-negative intracellular diplococci.

### PATHOLOGIC FACTORS

After the early confusion as to the identities of syphilis and gonorrhea was cleared up [1] and after it was proved that vaginitis could be contracted innocently, the disease was described as an inflammation of the vulva and the vagina. Kenessey [34] in 1913 reported the postmortem examinations of 2 infants who died of postvaricella pneumonia, at the ages of 14 months and 10 months, respectively. The tissues showed all the characteristic inflammatory changes found in adults. Kenessey described typical salpingitis, oophoritis and pelvic peritonitis with all the usual plastic changes. From 1 of the patients he was able to culture the gonococcus. In the same year Rubin and Leopold [35] reported the inflamed appearance of the cervix found on direct examination. This has been confirmed by the majority of writers since then. In 1916 Hess [36] described observations made at 4 autopsies, which showed no vaginal reaction but a macroscopic and microscopic inflammatory reaction in the superficial and deep tissues of the vaginal portion of the cervix. He emphasized that he saw no evidence of endocervicitis. In 1927 Hamilton [6] reported that on autopsy he found the vaginal mucosa to be of the immature type with a typical inflammatory reaction which extended to the subepithelial tissues. Schauffler and Kuhn [37] stated that Bartholin and Skene glands remained as simple structures until puberty, that the cervix remained larger than the fundus uteri and contained none or poorly developed endocervical glands and that these tissues were not involved in the infection. Although they found frequent involvement of the vaginal portion of the cervix, which was covered by a thin layer of squamous epithelium as was the vagina itself, they denied that true endocervicitis occurred. On the other hand, Williams [38] described pus coming from the external os of the cervix, and in 95 per cent of his cases smears from the cervical canal were

34. Kenessey, A.: Pest. med.-chir. Presse **49**:360, 1913.

35. Rubin, I. C., and Leopold, I. S.: On the Cause of the Persistence of Gonorrheal Vulvovaginitis in Children, Am. J. Dis. Child. **5**:58 (Jan.) 1913.

36. Hess, A. F.: Provocative and Prophylactic Vaccination in the Vaginitis of Infants, Am. J. Dis. Child. **12**:466 (Nov.) 1916.

37. Schauffler, G. C., and Kuhn, C.: Am. J. Obst. & Gynec. **25**:374 (March) 1933. Schauffler, G. C.: Persistent Vaginal Discharge in Infants and in Little Girls: Cause and Treatment, Am. J. Dis. Child. **34**:644 (Oct.) 1927.

38. Williams, T. J.: Am. J. Obst. & Gynec. **16**:861 (Dec.) 1928.

positive. Gellhorn [39] stated the belief that endocervicitis sometimes occurred. Some writers [40] have expressed the opinion that the cervix is so frequently involved that the disease should be called cervicovaginitis. Iwanow [41] said that the vulva is the site of infection in most cases. From many biopsies he found that, although the mucous membrane may appear normal, organisms often are present in the deep tissues, even involving the muscular layers, with all the characteristic inflammatory reaction about them. Stein and his co-workers [17] stated the belief that the urethra and Skene's glands were often involved. TeLinde and Brawner [42] found no evidence of urethritis in their cases. Proctitis is considered by some to be so frequent that it is part of the disease. This, as well as other processes, will be considered under complications or separately.

### COMPLICATIONS

One author described complications as occurring chiefly in the literature. However, their occurrence cannot be doubted. The following tabulation gives the incidence of complications, as summed up from the reports of Spaulding,[43] Brown,[13] Gittings and Mitchell,[8] Notes,[15] J. R. Miller [44] and Barnett,[45] in a total of 565 cases.

| | |
|---|---|
| Urethritis | 14 |
| Proctitis | 12 |
| Arthritis | 15 |
| Tubal infection | 9 |
| Ophthalmia | 8 |
| Pelvic peritonitis | 5 |
| General peritonitis | 4 |
| Vulvovaginal abscess | 1 |
| Ischiorectal abscess | 1 |
| Inguinal adenitis with suppuration | 1 |

Bartholinitis has been described infrequently.[46]

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39. Gellhorn, G. J.: Use of Silver Nitrate Ointment in the Treatment of Vulvovaginitis in Children, J. A. M. A. **75**:1647 (Dec. 11) 1920.

40. Stein, Leventhal and Sered.[17] Norris and Mickelberg.[25] Brunet, Tolle, Scudder and Medcalf.[28]

41. Iwanow, N. S.: Arch. f. Gynäk. **155**:605, 1934.

42. TeLinde, R. W., and Brawner, J. N.: Am. J. Obst. & Gynec. **30**:512 (Oct.) 1935; discussion, ibid. **30**:887 (Dec.) 1935.

43. Spaulding, E. R.: Vulvovaginitis in Children, Am. J. Dis. Child. **5**:248 (March) 1913.

44. Miller, J. R.: Am. J. Obst. & Gynec. **29**:553 (April) 1935.

45. Barnett, N.: J. Obst. & Gynaec. Brit. Emp. **68**:600, 1913.

46. Norris and Mickelberg.[25] Spaulding.[43] Brown, J.: J. Iowa M. Soc. **24**:331 (July) 1934.

The incidence of urethritis cannot be determined from the literature. Williams,[38] Stein and his colleagues,[17] Pisacane,[20e] and Sharp [47] stated the opinion that it occurs frequently. Sharp gave the incidence as 50 per cent of her cases. Other writers have denied its occurrence.

Ascending infection through the tubes to the pelvic peritoneum occurs more often. Whether this spread is by means of the lymphatics or is direct we can only guess. Spaulding [43] said that abdominal pain suggests extension of the infection and that this occurs more frequently among older children. Phillips [48] obtained gonococci on direct peritoneal aspiration from a child who, suffering from gonorrheal vaginitis, complained of abdominal pain. Miller [44] wrote of finding salpingitis in children 5, 10 and 11 years old. Vogt [23] described a case of salpingitis and pelvic peritonitis found at operation. He expressed the belief that this complication occurs more frequently than is suspected. Gleich [49] reported a case of fulminating peritonitis in which smears showed the typical organisms and in which death occurred in twenty-four hours. Schauffler and his co-workers [50] had 9 such cases among 189 children with vaginitis. Lees [51] reported that 5.5 per cent of his patients had this complication. In 1934 Harris and Berman [52] surveyed the literature for gonorrheal peritonitis in young girls and found 34 cases. They added 2 cases to the list. When operation was resorted to the mortality was 50 per cent, while if conservative measures were used it was 24 per cent. In Brown's [13] patients a pelvic abscess formed which drained through the vagina.

Arthritis occurs rather infrequently.[53] It differs in no way from the same complication in adults.

Le Guay [54] and Grenet [55] described a case of gonorrheal septicemia in a child with vaginitis. Septic endocarditis and meningitis developed in this patient.

*Proctitis.*—There seems to be considerable confusion as to the incidence of proctitis in this disease. Valentin,[56] in 1921, found a high incidence of recurrence of infection after apparent cure. She inves-

47. Sharp, B. B.: Brit. J. Ven. Dis. **6**:301 (Oct.) 1930.

48. Phillips, R. B.: New England J. Med. **213**:1026 (Nov. 21) 1935.

49. Gleich, M.: Gonococcal Peritonitis Complicating Gonorrheal Vulvovaginitis, J. A. M. A. **86**:748 (March 13) 1926.

50. Schauffler, G. C.; Duke, R.; Crynes, S. F., and Schauffler, C.: West. J. Surg. **42**:669 (Dec.) 1934.

51. Lees, D.: Edinburgh M. J. **35**:61 (May) 1928.

52. Harris, E. H., and Berman, R.: J. Pediat. **4**:59 (Jan.) 1934.

53. Notes.[15] Schauffler and others.[50]

54. Le Guay: Quelques complications de la vulvo-vaginite gonococcique des petites filles, Thèse de Paris, no. 379, 1930.

55. Grenet, H.: Gynécologie **30**:641 (Nov.) 1931.

56. Valentin, I. E.: Deutsche med. Wchnschr. **47**:628 (June 2) 1921.

tigated the patients and found gonococci in the rectum in 61 of 161 patients. Fraser [4] stated that this infection occurs in the vast majority of cases and is so frequent as to be considered part of the disease. Fifty-nine of his 63 cases fell into this group. Pisacane [20e] found only a few cases of proctitis, while Williams [38] could obtain no positive rectal smears among his patients. Schauffler and his colleagues [50] warned that positive rectal smears are difficult to obtain. Fessler [20f] expressed the opinion that the infection of the rectum is frequently associated with the original infection.

In 1933 Ruys and Jens [57] took rectal cultures and smears from 72 children with positive gonorrheal vulvovaginitis with the following results:

| | |
|---|---|
| Cultures positive and smears positive | 35 |
| Cultures positive and smears negative | 8 |
| Cultures positive and smears questionable | 8 |
| Cultures negative and smears negative | 16 |
| Cultures negative and smears positive | 3 |
| Cultures negative and smears questionable | 2 |

Their first series consisted of 17 cases—7 of acute and 10 of chronic vaginitis. Rectal cultures from all the patients were positive. The history of 3 of the patients was told in detail. In 2 cases the rectal cultures were positive for two months after the vaginal smears and cultures and the rectal smears had become negative, while in the third case the rectal smears and cultures remained positive for two months after the vaginal smears and cultures became negative. This, if substantiated, would have great significance in any explanation of the high incidence of recurrence after apparent cure of the disease. It was further stated that the organism could be found, even though there was no apparent inflammatory reaction of the rectal mucous membrane.

In a patient observed by us who had negative vaginal smears the rectal smear, taken through a proctoscope, was positive, in spite of the fact that the rectal mucosa seemed normal.

Bloomberg and Barenberg [58] reported their pathologic observations on both male and female infants with rectal gonorrhea, which appeared in epidemic form. In 2 children who had apparently been cured of this infection autopsy showed ulcerations extending even to the muscularis.

57. Ruys, A. C., and Jens, P. A.: München. med. Wchnschr. **80**:846 (June 2) 1933.

58. Bloomberg, M. W., and Barenberg, L. H.: Gonorrheal Proctitis as a Cause of Blood and Mucus in the Stools of Infants, Am. J. Dis. Child. **29**:206 (Feb.) 1925.

### RELATION OF OPHTHALMIA TO VAGINITIS

When one considers the high incidence of ophthalmia neonatorum, it is surprising that in adults and children gonorrheal ophthalmia does not occur more frequently. It is thought that the highly bactericidal lysozyme serves to protect the eyes and that it is not present during delivery. However, although ophthalmia neonatorum does occur in the first few days of life, vaginitis occurs infrequently at this time. Conversely, although gonorrheal ophthalmia may occur at any age, it is comparatively infrequent in young children, considering the great opportunity for infection.[59] In our previous summary of statistics giving the incidence of complications, there were records of 8 cases of ophthalmia among 565 patients.

B. Epstein [24] and A. Hamilton [1] told of two interesting experiments. A. Epstein placed secretion from the eyes of patients with ophthalmia neonatorum in the vulvas of 2 girls a few weeks old without inducing vaginitis, while Fraenkel placed pus from the vaginas of girls whose vaginal smears were positive in the eyes of three moribund patients without inducing ophthalmia. No significance has been placed on these experiments.

### ADULTHOOD AND SEQUELAE

There has been little investigation of the effect of gonorrheal vaginitis on the patient after she reaches puberty and enters the childbearing age. Various authors, after noting the complications and pathologic factors mentioned, have stated the belief that there is a definite hazard which extends past puberty. Vogt [23] suggested that sterility and extra-uterine pregnancy are more frequent among women who have had vaginitis as children than among those who have not. Miller [59c] stated that cervicitis in young virgins may be due to this disease. Dobszay [14] expressed the opinion that, although it has not been proved, there is a definite relation between vaginitis and the common illnesses of adult females. Wrana [33] suggested that sterility may be a result of late reinfection just prior to puberty. Bucura [60] told of a woman without history of previous intercourse who infected her husband with gonorrhea. Investigation led Bucura to believe that she had contracted vaginitis as an infant and had been a carrier of the disease ever since. We have mentioned the 2 girls attending our clinic in whom the infection persisted after the onset of menstruation. Fraser [4] stated that the ultimate anatomic damage cannot be estimated but that pinhole os, imperforate hymen and malformations of the vagina and adnexa are

59. (*a*) Witherspoon, J. T.: New Orleans M. & S. J. **85**:108 (Aug.) 1932. (*b*) Nabarro, D.: Brit. J. Ven. Dis. **6**:318 (Oct.) 1930. (*c*) Miller, C. J., in discussion on Witherspoon.[59a]

60. Bucura, C.: Wien. med. Wchnschr. **76**:117 and 1214, 1926.

probably sequelae. Vasiliv-Chebotarev [61] expressed the opinion that infantilism and sterility are of frequent occurrence. Endometritis, gynatresia, dysmenorrhea, infantilism, sterility and extra-uterine pregnancy are listed as possible sequelae.

Opposing these views are the reports of Hamilton [6] and Dooley.[5] Hamilton found that 11 former patients had been delivered with less than 1 per cent of complications. Dooley tried to locate all patients who had been treated at the Johns Hopkins Hospital for a definitely diagnosed gonorrheal vaginitis and who were 20 years old or older at the time of his investigation. He could trace only 32 patients—21 white and 11 Negroes. The majority of these patients had received incomplete treatment or none. Seventeen of them were married. Of these, 10 had had children, 2 were pregnant and 2 practiced contraception. Dooley found no evidence among them of sterility, extra-uterine pregnancy, increased incidence of leukorrhea or dysmenorrhea or any influence on the time of onset of menstruation.

## TREATMENT

On reviewing the literature, it appears that almost the entire pharmacopeia has been used in treatment without really satisfactory results. In addition to the various silver and other antiseptic douches, pastes and topical applications, the list includes diathermy, cauterization, heat in various forms, vaccines, filtrates and changing the bacterial flora and acidity of the vagina.[62] In 1933 Lewis [63] suggested the use of estrogenic substance, in the form of theelin, and reported good results in a small series of cases. We shall not go into the theory of this method of treatment but shall try to summarize the reports in the literature. It is interesting to note, however, that in 1922 Norris and Mickelberg [25] tried to change the type of the vaginal epithelium from immature to adult by exposure to air, while in 1926 Fraser [4] reported that when the vagina assumed a whitish membranous appearance gonococci disappeared. His opinion was that this indicates an increase in the thickness of the vaginal epithelium. Within a short time after Lewis' report, Brown,[64] Huberman and Israeloff,[65] Nabarro and Signy,[66] Reading,[67]

61. Vasiliv-Chebotarev, A.: Sovet. vrach. gaz., May 15, 1935, p. 732.

62. Fraser.[4] Brunet, Tolle, Scudder and Medcalf.[28] Crossen, R. J.: J. Pediat. **6**:82 (Jan.) 1935.

63. Lewis, R. M.: Am. J. Obst. & Gynec. **26**:593 (Oct.) 1933.

64. Brown, J.: Treatment of Gonorrheal Vaginitis in Immature Girls, J. A. M. A. **102**:1293 (April 21) 1934.

65. Huberman, J., and Israeloff, H. H.: Therapeutic Value and Effects of Amniotin in Gonorrheal Vaginitis in Children, J. A. M. A. **103**:18 (July 7) 1934.

66. Nabarro, D., and Signy, A. C.: Lancet **1**:604 (March 16) 1935.

67. Reading, B.: South. M. J. **28**:464 (May) 1935.

Goldberg and his co-workers,[68] Miller,[44] Phillips[48] and TeLinde and Brawner,[42] using amniotin or theelin in various ways, reported their results. Most of the reports were enthusiastic in their support of this method of treatment. However, a few of the authors just mentioned pointed out that this method does not solve the problem of recurrences. Phillips[48] and Nabarro and Signy[66] found that smears taken from 70 per cent of their patients became positive after the cessation of treatment. TeLinde and Brawner[42] reported that about 25 per cent of their patients had a recurrence but declared that they responded quickly to a second course of the medication. Miller[44] obtained good results in only 19 of 42 patients. Wrana[33] warned of the possible danger connected with the use of this treatment. Witherspoon[69] had no success with it and included as reasons for his objection to it that there is the possibility of danger to the ovary, that the cervicitis is not affected, that reactions occur and that the treatment is costly. Phillips[48] said that this method is a definite advance in the treatment of the disease but that modification of the method is necessary.

At our clinic 66 of 80 patients were "cured" by this method of treatment. Only 7 of these proved to have negative smears on their last visit to the clinic, and only 2 had been seen for a sufficiently long period to be considered cured.

### DURATION OF THE DISEASE

Gonorrheal vaginitis is a chronic disease with periods of exacerbation and quiescence. It lasts from a comparatively short period in some children to years in others. In 1 of our cases the first positive smear was reported in 1929. Hamilton[6] stated the belief that the chronicity is due to three factors, namely, (*a*) the lack of the bacillus of Döderlein before puberty, (*b*) the absence of the normal acid reaction of the adult vagina and (*c*) the immature squamous epithelium present before puberty. Others have expressed the opinion that the chronicity of the disease is due to the fact that children may become carriers and the disease break out with each lowering of the general body resistance. Still other investigators have placed emphasis on the importance of hidden and untreated foci, such as the cervix, the urethra and the rectum, which serve to reinfect the vagina when treatment is stopped.

### REINFECTION

Reinfection is the bugbear in the treatment of this disease. Actually there is no evidence to show whether what takes place is a reinfection

68. Goldberg, L. E., and others: J. Pediat. **7**:401 (Sept.) 1935.

69. Witherspoon, J. T.: Treatment of Gonorrheal Vulvovaginitis in Childhood with the Ovarian Follicular Hormone, Am. J. Dis. Child. **50**:913 (Oct.) 1935.

from some outside source or a recurrence or recrudescence of the original infection. With or without treatment, vaginal smears tend to become negative after a variable length of time, and later the discharge reappears and smears become positive. So frequently does this occur that some authors have expressed the opinion that the disease cannot be cured. Spaulding [43] had 24 recurrences among 26 cases. Norris and Mickelberg [25] reported recurrences in 12 per cent of their patients; Schauffler and his colleagues,[50] in 25 per cent; Notes,[15] in 6 per cent, and Williams,[38] in 23 per cent. Gumpert,[70] Miller [44] and Valentin [56] had frequent recurrences among their patients. Schauffler and his co-authors [50] stated that "Whereas the vast majority of initial vaginal infections are contracted from other infected individuals . . . reinfection is seldom so contracted." They expressed the belief that inanition, intercurrent diseases, fatigue, proctitis, cervicitis, pinworms and masturbation are factors in the high incidence of recurrence. Hess [36] suggested that carriers may be responsible for reinfection, while Norris and Mickelberg [25] blamed the urethra, cervix and Bartholin glands. Fessler [20f] stated that relapses may be due to rectal infection. Before any form of treatment will be successful it is essential that these questions be solved.

### LATENCY

That the disease can be present in a latent stage, as in adults, was suggested by Hess,[36] B. Epstein,[24] Wollstein,[70a] Sinclair [71] and Wrana.[33] Terwilliger,[72] while using vaccines for the treatment of the disease, found that in 2 of his control patients, who apparently had been free from the disease, a gonorrheal vaginal discharge had suddenly developed. Scudder [73] found that persons with latent vaginitis had negative vaginal smears and cultures. Some authors have proposed using vaccines and other materials as provocatives in order to prove cures and also to discover carriers and those having the disease in a latent phase in time to prevent their admission to general hospital wards.

### CRITERIA OF CURE

There are no standard criteria of cure in general use. Some physicians accept as sufficient evidence a few consecutive negative vaginal smears, with or without treatment of the patient, while others insist on prolonged check-ups and the use of provocatives to prove the cure. Fraser's [4] criteria were: (*a*) three consecutive negative smears at two

70. Gumpert, M.: Deutsche med. Wchnschr. **57**:155 (Jan. 23) 1931.
70a. Wollstein, M.: J. Obst. & Gynaec. Brit. Emp. **68**:607, 1913.
71. Sinclair, J. F.: J. Obst. & Gynaec. Brit. Emp. **68**:1210, 1913.
72. Terwilliger, W. G.: Canad. M. A. J. **25**:294 (Sept.) 1931.
73. Scudder, S. A.: J. Urol. **14**:429 (Nov.) 1925.

week intervals, without treatment; (*b*) a rest for two months, after which a vaccine was injected and cultures and smears were taken from the cervix, vagina, vulva, urethra and rectum, and (*c*) a rest for three months, after which the injection and the taking of cultures and smears were repeated. Norris and Mickelberg [25] took smears and examined the patient with the endoscope at two week intervals for six weeks. This was repeated after one month and again after three months. Fessler [20f] used irritating substances and finally milk injected intracutaneously to prove a cure.

Our criteria at present consist of three consecutive negative vaginal smears while the patient is under treatment, followed by four weekly negative smears and then six monthly negative smears after treatment has ceased.

### METHODS OF PROPHYLAXIS AND CONTROL

Prophylaxis in the sense of the use of some chemical to inhibit and prevent an infection has received no attention except in regard to the new-born. For them various silver preparations to be instilled into the vulva have been suggested. In hospitals, isolation and strict precautions against contagion have been relied on to control the spread of the disease. Even a superficial review of the literature shows that in the main this has not been quite successful in preventing the appearance and spread of the infection. So baffling is this fact to observers that it has been suggested that there may be a separate disease or a particular strain of the organism which is epidemic.

In the home prophylaxis consists, first, in the education of the adults and infected persons.[47] Practically, this is a difficult procedure. Infection in the male is easily detected, and he can be taught the necessity of cleanliness. But the woman who has gonorrhea, especially if the attack is a mild one, does not seek treatment, and when the infection reaches a chronic stage an absolute diagnosis often cannot be made. For this reason a great many women suffering from gonorrhea never suspect their true condition, receive no instruction concerning the precautions they should take and are at great loss to explain the presence of the infection in their daughters. Second, if the disease appears in one of the girls in a family, strict precautions must be taken to prevent the infection of the other girls. In our experience, it has been the rule that when one girl in the family has the disease all the others will have positive vaginal smears.

Taussig [74] stated the opinion that toilet seats are a frequent source of spreading the disease. He advised the use of low U-shaped toilet seats. Epstein,[24] believing that the infection occurs at birth, declared that prophylaxis lies in treating the disease in the mother. The majority

74. Taussig, F. J.: Am. J. Obst. & Gynec. **30**:889 (Dec.) 1935.

of writers advise exclusion of infected children from school as a public health measure. On the other hand, Nelson [12] said that until one can prove that children going to school are possible sources for the spread of gonorrheal vaginitis there is no basis for imposing such exclusion.

Oppenheimer and Everett [8] surveyed methods of general control in Washington, D. C., and found that there was no coordination whatever. Apparently the only method generally attempted was the exclusion of infected children from school. Even this measure was not properly carried out, for some children who were supposed to be excluded were attending school while others were staying out of school for long periods although they received no examination to ascertain whether smears were still positive.

### EXCLUSION OF INFECTED CHILDREN FROM SCHOOL AND THE SOCIAL AND THE PSYCHOLOGIC ASPECTS

The social aspect of the disease has received scant attention. There are only occasional articles which describe home conditions, the high incidence in poor families, the problem of exclusion from school and the stigma attached to the disease. Gumpert [70] and von Zumbusch [11] described special classes for infected children, with teachers who have considerable knowledge of the disease. They cautioned against teachers who, knowing nothing about the disease, either belittle or exaggerate its importance, with a corresponding bad psychologic effect on the pupils. Wehrbein [7] reported a high incidence of behavior problems in her group. Medcalf [75] and Oppenheimer and Everett [8] described home conditions among their patients.

### SUMMARY

The problems of diagnosis, complement fixation and vaginal acidity and the importance of the bacillus of Döderlein have not been reviewed in this paper. Treatment has been discussed only briefly because as yet a generally accepted and successful method of treatment is not available.

In our introduction we stated certain questions which required answers. According to our present knowledge, as found in the literature, we can in most cases give only incomplete answers.

1. *Actual Incidence.*—The true incidence of this infection is unknown but is probably much larger than is suspected.

2. *Source of Infection.*—The infection is usually contracted from adults, but young sisters and playmates also frequently spread the disease. Rape is an infrequent source of infection. The part played by toilet seats and other infected objects can only be guessed.

75. Medcalf, in Brunet, Tolle, Scudder and Medcalf.[28]

3. *Age Limits.*—The infection rarely occurs at birth and usually does not persist after puberty. Exact knowledge concerning possible inhibiting factors present at these age extremes is lacking. The disease is most frequent between the ages of 3 and 10 years.

4. *Period of Contagiousness.*—It is not known how long an infected child remains a menace to other children. The spread of infection from child to adult has not been reported in the literature. At present infectivity is considered to be present as long as gonococci can be found in the vaginal smear. Nothing appears to be known about the importance of carriers.

5. *Causative Agent.*—The organism causing gonorrheal vaginitis in children is unquestionably the same which causes gonorrhea in adults, although the infection is possibly less virulent in the child.

6. *Pathologic Factors.*—There is considerable disagreement concerning the usual pathologic processes involved. The infection apparently involves both the superficial and the deep tissues of the vulva, the vagina and the vaginal portion of the cervix. Bartholin's glands, Skene's glands and the endocervix probably are not involved, at least in the majority of cases. Further, the involved tissues may show no superficial evidence of infection, although the organisms may be found in the underlying structures.

7. *Complications.*—Complications do occur but are infrequent. They may be severe enough actually to threaten the life of the patient.

8. *Relation of Ophthalmia to Vaginitis.*—Ophthalmia only infrequently follows vaginitis. Nothing but theories can be offered to explain the protection either of the vagina or of the eyes at different periods of life. This protection, however, is only relative.

9. *Incidence of Proctitis and Urethritis and Their Relation to Recurrence.*—There is no agreement as to the incidence of proctitis or of urethritis. The former probably occurs frequently. The relation of these conditions to the question of recurrence is important.

10. *Recurrence.*—No distinction can be made at present between recurrence and reinfection. It is true that the children treated by outpatient services are constantly in the environment which produced their initial infection. However, in hospitals where isolation has been practiced recurrences have taken place.

11. *Latency and Carriers.*—As among adults, patients in whom the disease is latent and carriers of the disease are probably to be found among children, although there is no way of knowing how frequently.

12. *Adulthood and Sequelae.*—In spite of reports to the contrary, a certain small percentage of the patients probably suffer sequelae after the age of puberty because of complications which occurred while

they were children. What percentage of such children carry the infection as an active disease past the age of puberty is unknown.

13. *Criteria of Cure.*—There are no acceptable criteria of cure in general use. For that reason statistics on cures with various forms of treatment are unreliable.

14. *Methods of Prophylaxis and Control.*—Except for the general methods of prophylaxis used for any contagious disease, no way of preventing the spread of the infection is known.

15. *Exclusion of Infected Children from School and the Social and the Psychologic Aspects.*—The problem presented by the exclusion of infected children from school and the other social and psychologic problems arising from the existence of the disease will be solved only when its importance is recognized. It will require the cooperation of the social service organizations, of the local boards of health and of education and of the medical profession to deal with them successfully.

## RECOMMENDATIONS

It is apparent that many recommendations may be made. We feel, however, that if certain proposals were carried into effect a foundation for all future control of the disease would be established. It is for that reason that we limit ourselves to proposing the following measures:

1. The formation of criteria for the diagnosis and cure of vaginitis which would be generally accepted. This would allow justifiable comparison of all therapeutic methods.

2. The establishment of a central clearing bureau preferably under the authority of the local board of health. Here permanent records would be kept under the separate title of "vaginitis of children." Each child's card would carry data indicating that she was undergoing treatment, that she was excluded from school while her smears were positive and that her contacts were being examined. Such records would give a real insight into the problems mentioned and provide accurate statistics.

3. More cooperation among workers in this field, with the object of establishing standards and preventing duplication of work.

# News and Comment

## GENERAL

**Physicians Certified by American Board of Pediatrics.**—The following physicians have been certified by the American Board of Pediatrics since the last report:

John Bernard Ahouse, Yonkers, N. Y.; Morris Astrachan, Brooklyn; Hilde Bruch, New York; Frederick Castrovinci, New York; Stewart H. Clifford, Brookline, Mass.; Robert W. Culbert, New York; Charles S. Culotta, New Haven, Conn.; Katharine G. Dodge, New York; Elvira Goettsch, New York; Arthur Heyman, Newark, N. J.; Henry W. Kaessler, Bronxville, N. Y.; Jacob Kalish, Brooklyn; Morris Y. Krosnick, New Haven, Conn.; Milton Isra Levine, New York; Donovan James McCune, New York; Rosa Lee Nemir, New York; Antoinette Raia, Jackson Heights, N. Y.; Margaret Ruth Reynolds, Jackson Heights, N. Y.; Hyman Rubinstein, Brooklyn; Harry J. Seiff, New York; Abraham Tow, New York; H. Beril Warshall, Brooklyn; Paul G. Albrecht, Cleveland; Samuel A. Anderson Jr., Richmond, Va.; W. Dulaney Anderson, Chattanooga, Tenn.; John Aull, Kansas City, Mo.; E. W. Barron, Columbia, S. C.; Frederic H. Bartlett, New York; Benjamin Bashinski, Macon, Ga.; Reuel A. Benson, New York; Joseph Vincent Bergin, Paterson, N. J.; Hugh Kling Berkley, Los Angeles; Charles James Bloom, New Orleans; David Hartin Boyd, Pittsburgh; O. F. Bradford, Columbia, Mo.; Morris L. Bridgeman, Portland, Ore.; Alan Brown, Toronto, Canada; Charles R. Bugg, Raleigh, N. C.; Charles Wason Burhans, Lakewood, Ohio; Joseph Alexander Bybee, Beaumont, Texas; Randolph K. Byers, Boston; Joseph K. Calvin, Chicago; Walter Lester Carr, New York; Jerome Cochran Chapman, Birmingham, Ala.; Arch. B. Chappell, Middletown, N. Y.; Irving Claman, New York; George Becker Cornick, San Antonio, Texas; Howard Reid Craig, New York; Lyman Ray Critchfield, St. Paul; William R. Cross, Knoxville, Tenn.; Jean Crump, Philadelphia; George McClave Cultra, Amarillo, Texas; John C. Danahy, Clincinnati; Daniel Cady Darrow, New Haven, Conn.; Tom Forest Davenport, Atlanta, Ga.; Ethel M. Davis, Chicago; Roger William Dickson, Atlanta, Ga.; Henry Dietrich, Los Angeles; Thomas Davis Dotterer, Columbia, S. C.; Hugh L. Dwyer, Kansas City, Mo.; Charles Judson Eldridge, Kansas City, Mo.; Lewis W. Elias, Asheville, N. C.; Henry C. Flood, Pittsburgh; Arthur Petherick Foreman, Syracuse, N. Y.; Morgan Jacob Foster, Cedar Rapids, Iowa; Justin Allis Garvin, Cleveland; Clain Fanning Gelston, San Francisco; John Giblin, New York; Louie Oscar Godley, Fort Worth, Texas; Nathan Gorin, Boston; Gaylord Willis Graves, New York; Berryman Green, Riverside, Calif.; Leonard H. Greenbaum, Los Angeles; Joseph Greengard, Chicago; Francis J. Gustina, Buffalo; Clark H. Hall, Oklahoma City; John C. Hamilton, New York; Margaret I. Handy, Wilmington, Del.; Theodore Hudson Harrell, Mission, Texas; L. P. Harsh, Akron, Ohio; Francis Bernard Hart, Brooklyn; Joyce I. Hartman, Cleveland; Harold Herman, New York; Johanna Heumann, Chicago; Miner C. Hill, New York; Russell R. Hippensteel, Indianapolis; Gerald Norton Hoeffel, Boston; Luther William Holloway, Jacksonville, Fla.; Elmer Grant Horton, Columbus, Ohio; Philip J. Howard, Detroit; Henry Eugene Irish, Chicago; Joseph Andrew Johnston, Detroit; Basil Bradbury Jones, Richmond, Va.; Marion Yates Keith, Greensboro, N. C.; Dennis H. Kelly, Des Moines, Iowa; John M. Lee, Nashville, Tenn.; Edith M. Lincoln, New York;

Harry R. Lohnes, Buffalo; Alexander Tertius Martin, New York; Charles Marcellus Mashburn, Atlanta, Ga.; W. Frederick Mayer, Johnstown, Pa.; Hugh McCulloch, St. Louis; Kenneth M. Metcalf, New York; Edith M. Meyers, Oakland, Calif.; Myrl Milton Miller, Akron, Ohio; John McK. Mitchell, Rosemont, Pa.; Harold Ruckman Mixsell, New York; Cecile R. Moriarty, Minneapolis; Edwin R. Murphy, Salt Lake City; Lewie H. Muse, Atlanta, Ga.; William S. O'Donnell, Detroit; George F. Patterson, Cincinnati; Jack Furman Perkins, Dallas, Texas; Giuseppe Previtali, New York; Harold W. Price, Calgary, Canada; James Joseph Reilly, Camden, N. J.; George Renner, Jr., Cincinnati; George Mathew Retan, Syracuse, N. Y.; Frank Howard Richardson, Black Mountain, N. C.; Fred Rittinger, Cleveland; Worth Ross, Detroit; Charles L. Ruggles, Cleveland; Harold O. Ruh, Cleveland; Robert Salinger, New Haven, Conn.; Arthur Saul Sandler, Chicago; Saul Schlegman, White Plains, Ill.; Oscar M. Schloss, New York; John Ansel Schoonover, Denver; Louis H. Segar, Indianapolis; Frank Seinsheimer, Cincinnati; Theodore King Selkirk, Cincinnati; W. Ray Shannon, St. Paul; Jeremiah T. Simonson, New York; John William Simpson, Birmingham, Ala.; William Ewing Sinclair, Orlando, Fla.; Raymond M. Sloan, Huntington, W. Va.; Charles Hendee Smith, New York; Arnold Miller Smythe, Des Moines, Iowa; Susan Page Souther, Hartford, Conn.; William St. Lawrence, New York; Walter Steoffler, Indianapolis; Claudius A. Street, Winston-Salem, N. C.; Robert Alexander Strong, New Orleans; William Walfred Swanson, Chicago; Leo M. Taran, Brooklyn; Caleb O. Terrell, Fort Worth, Texas; Frederick Fitzgerald Tisdall, Toronto, Canada; Joseph M. Ulrich, Akron, Ohio; Henry E. Utter, Providence, R. I.; Frank Van Schoick, Jackson, Mich.; Lynn B. Vaughan, Long Beach, Calif.; William Wirt Waddell Jr., Charlottesville, Va.; Samuel Patrick Wainright, Birmingham, Ala.; J. LaBruce Ward, Asheville, N. C.; Richard Gwyn Watson, Oakland, Calif.; Stewart H. Welch, Birmingham, Ala; Stanley M. Wershof, New York; Theodore S. Wilder, Germantown, Philadelphia; Charles Alexander Wilson, Detroit; Franklin Davis Wilson, Norfolk, Va.; John Armstead Winstead, Rocky Mount, N. C.; Alfred Maximilian Wise, Brooklyn; Ernst Wolff, San Francisco; Byron Parker York, Houston, Texas; James Herbert Young, Boston; Paul J. Zentay, St. Louis; Edmund R. McCluskey, Pittsburgh; Ellsmer Landis Piper, Pittsburgh.

Twenty-two of these physicians were examined, and at that examination ten physicians failed.

# Abstracts from Current Literature

## Anatomy and Embryology

THE VITAMIN C TECHNIQUE AS A CONTRIBUTION TO CYTOLOGY. G. BOURNE, Anat. Rec. **66**:369 (Oct. 25) 1932.

Györgyi showed that adrenal tissue caused precipitation of silver nitrate. The precipitating agent was called hexuronic acid. Later it was shown to be cevitamic acid. Using various tissues, Bourne has shown that many diverse types of cells precipitate silver nitrate if one uses the solution of Giraud and Leblond. He believes that this solution will help in studying cells and cell metabolism.

SNELLING, Toronto, Canada.

## Biochemistry; Bacteriology, and Pathology

SOME RECENT ADVANCES IN VACCINES AND SERUMS. L. D. FOTHERGILL, M. Clin. North America **19**:1409 (March) 1936.

Some recent experiments on transmission of whooping cough have convinced Fothergill that Haemophilus pertussis is the sole etiologic agent. Pertussis vaccine as prepared by Sauer represents an immunizing agent, and its use is justified for this purpose only. There is no justification for the use of any pertussis antigen or vaccine as a therapeutic agent.

Placental extract is capable of preventing or modifying measles. The substances responsible for this action do not differ from those contained in convalescent serum.

Ramon's original tetanus toxoid has recently been improved, an alum-precipitated product having been obtained which is retained in the tissues longer, causes fewer reactions and produces immunity with one dose. This immunity, however, develops slowly, reaching its maximum in from three to five months, and is maintained for from twelve to eighteen months. Secondary stimulation of previously immunized persons by another dose of toxoid leads to a prompt and very rapid rise in serum antitoxin.

As to meningococcic antitoxin (Ferry), Fothergill believes that sufficient evidence has not been advanced to prove that the meningococcus produces a true soluble exotoxin. This organism is, however, susceptible to autolysis, with the liberation of endotoxin, especially when grown on a fluid medium. Immunization with such filtrates would result in the production of antiendotoxin, which need not be any different from the antibacterial serum produced by the usual methods of immunization with meningococci. Fothergill feels that Ferry's so-called antitoxin is such a serum. He does not claim that it is without value but believes that it is not different from the usual antimeningococcic serum.

Following a critical summary of recent laboratory and clinical investigations concerning staphylococcic toxoid and antitoxin, the opinion is expressed that the toxoid is a useful agent in the treatment of chronic staphylococcic infections of the skin, that if results are not obtained after a short period of treatment there is no point in continuing the treatment, that staphylococcic antitoxin may relieve certain symptoms and may, in some cases of acute septicemia, prevent early death, that it has little curative value in subacute or chronic pyemia and osteomyelitis that it has no demonstrable bactericidal effect, and that its therapeutic usefulness is limited.

EUGENE SMITH, Ogden, Utah.

A Cultural Method for Classifying Staphylococci as of the "Food Poisoning" Type. R. V. Stone, Proc. Soc. Exper. Biol. & Med. **33**:185 (Oct.) 1935.

So far, the human being is the only reliable test animal for determining the presence of staphylococci in instances of food poisoning. Investigations indicate that protein is the only consistent major ingredient of the food involved in every outbreak. Seventy strains of staphylococci isolated from different sources were studied. The enterotoxic strains gave positive results (liquefaction of gelatin), and the others (pyogenic, septicemic, saprophytic, dermatoxic, hemolytic, lethal) gave negative results.

The preparation of beef extract gelatin is described. A culture of staphylococci is made and incubated at 37.5 C. for twenty-four hours. Any degree of liquefaction evidences the presence of a food poison staphylococcus. No liquefaction is present in negative strains.

Hansen, Minneapolis.

Influence of Magnesium Oxide on Antipyretic Action and Toxicity of Acetylsalicylic Acid in Rabbits. D. R. Climenko, Proc. Soc. Exper. Biol. & Med. **34**:807 (June) 1936.

Given quantities of acetylsalicylic acid and magnesium oxide have no antipyretic effect when administered separately but have a marked antipyretic action when given together. The toxicity of acetylsalicylic acid is not influenced by the magnesium oxide. The toxicity of a mixture with 50 per cent acetylsalicylic acid and 50 per cent magnesium oxide is half as great as the toxicity of the amount of acetylsalicylic acid which is required to produce the same therapeutic effect.

Hansen, Minneapolis.

Lactic Acid Bacilli from the Vagina, the Nursling's Intestine and the Teeth. Heinz Reploh, Zentralbl. f. Bakt. (Abt. 1) **133**:332, 1935.

Lactic acid bacilli were isolated from the vaginas of normal pregnant women, from carious teeth and from stools of nurslings in broth containing 2 per cent dextrose and 0.5 per cent acetic acid. The cultures were compared in various ways. Reploh could find no typical differences and concludes that they are all essentially of the Bacillus acidophilus group.

Paul R. Cannon. [Arch. Path.]

Dangers of Large Doses of Grenz Rays. Mathilde Kolrep, Ztschr. f. Kinderh. **55**:546, 1933.

According to Kolrep, grenz rays are not entirely harmless to young growing rats. In large doses these rays inhibit the growth of the bone. The application of 2,000 roentgens may be injurious, but from 3,000 to 3,500 roentgens always impairs growth of the bone.

Levinson, Chicago.

## Metabolism; Infant Feeding; Milk and Other Foods

Importance of Certified Milk in the Diet After Infancy. H. L. Dwyer, Arch. Pediat. **53**:635 (Sept.) 1936.

Dwyer considers certified milk of greater value in the diet of the older child than in that of the infant.

Orr, Buffalo.

Study of Cholesterol Fractions in Acute Infections of Infants with and Without Eczema. A. V. Stoesser, Proc. Soc. Exper. Biol. & Med. **34**:10 (Feb.) 1936.

Fourteen infants ranging in age from 3 to 13 months were studied, six of them having infections of the upper respiratory tract but no eczema, three having

eczema with repeated acute infections of the respiratory tract, and the other five having severe pneumonia. Samples of blood were collected during the height of the disease and after the seventh day of normal temperature. The total cholesterol values for the infants studied were lower during the acute infection than during the period of convalescence, this being due to a decrease in the cholesterol ester. The changes which occurred were not as marked in the infants as in the older children. This is especially true of patients with eczema. However, for the babies with pneumonia the cholesterol value during the height of the illness was less than 100 mg. per hundred cubic centimeters in the majority of the cases and returned to a higher level during recovery.

HANSEN, Minneapolis.

AN INVESTIGATION OF THE DIET OF SCHOOL CHILDREN. A. ANDERSON, Brit. M. J. **1**:1221 (June 13) 1936.

This is a discussion of a survey made by the author, pointing out the deficiencies in the diet of school children.

ROYSTER, University, Va.

REGULATION OF WATER METABOLISM THROUGH THE CENTRAL NERVOUS SYSTEM. L. RIBADEAU-DUMAS and LE MELLETIER, Nourrisson **24**:129 (May) 1936.

In support of the view that the hypothalamus has much to do with water metabolism is cited the case of an infant aged 4 months who died after three attacks of vomiting and diarrhea, recurring at short intervals. The last attack was accompanied by convergent strabismus, inequality of the pupils and nystagmus. The spinal fluid was normal, but necropsy revealed basilar meningitis with thickening of the arachnoid covering the optic chiasm. Pressure on the hypothalamus with inflammation is offered to explain the recurring attacks of vomiting and diarrhea. The middle ears and mastoids showed no pathologic changes.

McCLELLAND, Cleveland.

VEGETABLES IN INFANT FEEDING. RENÉ MATHIEU, Rev. franç. de puériculture **3**:159, 1935.

Vegetables fed with milk or with buttermilk provide a diet rich in minerals and vitamins, which will cure or prevent: (1) intestinal infantilism, a rare but serious malady, (2) cow's milk dyspepsia, and (3) the anorexia of the second half of the first year, a syndrome extraordinarily common in Paris. If one starts feeding vegetables early, about the fourth month, and if one does not give cow's milk in too great quantities or abuse the use of sugar and cereals, one will obtain remarkable results. Powdered vegetables facilitate administration. Mathieu regrets that vegetables are not more generally used in the feeding of infants in France.

CRANE, Chicago.

A CLINICAL STUDY OF THE ANTIGALACTOGENIC EFFECT OF CAMPHOR IN OIL. G. A. C. DE MAGALHAES, Rev. de gynec. e d'obst. **30**:773 (Oct.) 1936.

De Magalhaes found that intramuscular injections of camphorated oil decreased the flow of milk and did not seem to cause local discomfort. Two local applications a day of 10 per cent camphorated petrolatum had a similar action.

SANFORD, Chicago.

COMPOSITION OF BREAST MILK FROM MEXICAN MOTHERS. MARIA DE LA LUZ ESCONTRIA, Rev. mex. de puericultura **5**:875 (Nov.) 1934.

The normal composition of the breast milk from Mexican mothers taken from one hundred observatons is as follows: density, 1.0328; index of refraction, 47.9; acidity, 0.032 per cent; aldehyde index, 1.53 per cent; casein, 0.75 per cent; total nitrogen, 0.179 per cent; protein, 1.14 per cent; albumin, 0.374 per cent; lactose, 8.07 per cent; fat, 3.25 per cent; dry extract, 12.44 per cent; ash, 0.157 per cent; chlorides, 0.038 per cent; phosphates, 0.057 per cent.

Mexican breast milk is more dense, the lactose content is higher and the protein and ash contents are lower as compared to breast milk from Europeans.

HERRON, Spokane, Wash.

DIET FOR CHILDREN WITH FEVER. LISELOTTE MEYER, München. med. Wchnschr. **83**:1057 (June 26) 1936.

A suitable diet for children with fever is one that has sufficient calories, is easily taken by the patient, has as beneficial an effect as possible and is simple and cheap. The cost is important for most persons, especially those on relief. Large quantities of protein should not be given during fever. For infants Meyer advises a quart of 10 or 15 per cent sugar water with raw fruit or vitamin C tablets. After three days half an egg yolk is added. When the patient has been afebrile several days, from 3 to 10 ounces (90 to 300 cc.) of milk is given.

BRAHDY, Mount Vernon, N. Y.

DIGESTION IN INFANTS: XVII. BILE ACTIVATOR OF PROLIPASE IN HUMAN MILK. E. FREUDENBERG, Ztschr. f. Kinderh. **55**:714, 1933.

It is shown by Freudenberg that the prolipase of human milk is activated by cholic, taurocholic, glycocholic and other cholic acids but not by lithocholic acid.

LEVINSON, Chicago.

SPONTANEOUS HYPOGLYCEMIA IN CHILDREN. EINAR LENSTRUP, Ugesk. f. læger **98**:481 (May 28) 1936.

A 2 year old boy was brought to the hospital in a comatose state. The face was flushed but not cyanotic. The body was relaxed; there was no stiffness of the neck; Kernig's and Brudzinski's signs were absent; slight spasms were noted in the arms and legs. The condition seemed to indicate diabetic coma. The blood sugar was found to be 50 mg.; i. e., there was marked spontaneous hypoglycemia. Instillation of 50 cc. of a 10 per cent solution per rectum was followed by very rapid recovery.

Lenstrup reviews the literature and calls attention to the fact that this condition is rather common.

ELGHAMMER, Chicago.

## Vitamins; Avitaminoses

RELATIONSHIP OF VITAMIN C TO THE HEMORRHAGIC DIATHESES. D. J. STEPHENS and E. E. HAWLEY, J. Lab. & Clin. Med. **22**:173 (Nov.) 1936.

The effect of large doses of vitamin C was studied in four patients with hemophilia and in two with chronic thrombocytopenic purpura. This therapy apparently had no effect on the hemorrhagic manifestation, the blood picture or the capillary resistance. It is suggested that favorable therapeutic effects from vitamin C will be found only in those cases of capillary bleeding in which deficiency of vitamin C is present.

MCMURRAY, Galveston, Texas.

AVITAMINOSIS: XVII. INFLUENCE OF HIGH FAT-CONTAINING DIETS ON VITAMIN B REQUIREMENTS. B. SURE and K. S. BUCHANAN, Proc. Soc. Exper. Biol. & Med. **33**:75 (Oct.) 1935.

It has been previously reported (Sure, B.: *Proc. Soc. Exper. Biol. & Med.* **30**:622, 1933) that as much as 30 per cent of fat in the diet has no sparing action on vitamin B requirements for lactation in rats. In this study with five groups of rats, neither increasing the fat nor increasing the proteins in the rations containing an abundance of vitamin B was followed by any noteworthy sparing action on vitamin B requirements of the nonlactating albino rat. Thus, these results indicate that high fat diets have no sparing action on vitamin B requirements, even with an abundance of protein and vitamin G.

These findings agree with those of Steenbock and Kemmerer (*Bulletin* 428, *Wisconsin Experiment Station, Report* 27) but not with those of Evans and Lepkowsky (*J. Biol. Chem.* **107**:429, 1934). HANSEN, Minneapolis.

ENZYMIC EFFICIENCY IN AVITAMINOSIS. B. SURE, M. C. KIK and K. S. BUCHANAN, Proc. Soc. Exper. Biol. & Med. **33**:78 (Oct.) 1935.

Previous studies by Sure, Kik and Buchanan (*J. Biol. Chem.* **108**:19, 1935) revealed in vitamin B deficiency a marked reduction in the efficiency of digestive action of pancreatic lipase but no demonstrable disturbance in that of trypsin or erepsin. In vitamin B deficiency a great decrease in the value for pancreatic lipase and esterase activity and an increase in serum phosphatase occurred. In vitamin A deficiency, a decrease in blood serum esterase and an increase in hepatic lipase were found. So far as the relation of vitamins to digestion is concerned, the only influence found to date is the marked decrease in efficiency of digestion of fats in vitamin B deficiency. HANSEN, Minneapolis.

CAPILLARY FRAGILITY AND VITAMIN C. G. K. ANDERSON, E. E. HAWLEY and D. J. STEPHENS, Proc. Soc. Exper. Biol. & Med. **34**:778 (June) 1936.

Capillary fragility was measured by applying a vacuum cup with various amounts of negative pressure to the inner surface of the upper arm. Considerable variation in capillary resistance was found in normal subjects. Variation in the vitamin C intake of normal persons had no significant effect on the capillary resistance. HANSEN, Minneapolis.

LESIONS OF THE CENTRAL AND PERIPHERAL NERVOUS SYSTEMS PRODUCED IN YOUNG RABBITS BY VITAMIN A DEFICIENCY AND A HIGH CEREAL INTAKE. EDWARD MELLANBY, Brain **58**:141, 1935.

Most of the previously published experimental work on vitamin A deficiency and a high cereal intake was done on dogs. In the present investigation the author used rabbits, feeding them a diet containing bran, oats and calcium carbonate. Dried alfalfa in which the carotene content had been destroyed was also added. Lesions of the nervous system do not appear if alfalfa is fed in which the carotene content is not destroyed. The less the carotene content, the more intense the lesion and the more rapid its development. Ergot was given at first, but it was decided that most, if not all, of the specific lesions of the nervous system could be readily produced without giving ergot or its derivatives. Control animals were maintained in a healthy state by adding the protective factor to the same basal diet as that given to the affected animals.

Young rabbits grow and remain well on the basal diet for some months. Slight stiffness of the legs, xerophthalmia and characteristic movements of the head, as if the animal did not know its position in relation to the rest of its body, develop in the order named. There is no definite paralysis, but the animals appear heavier on their legs and show fewer spontaneous movements.

Histologic studies were made of the spinal cord, brain stem and peripheral nerves. In the spinal cord degeneration was found in the following ascending paths: the dorsal columns and the dorsospinocerebellar, ventrospinocerebellar, lateral spinoreticulothalamic, spinotectal and ventral spinoreticular thalamic tracts and possibly the spino-olivary tract. Of the descending tracts, degenerated fibers were found in the rubrospinal, vestibulospinal and dorsal longitudinal bundles. The main descending tract, the crossed pyramidal tract, occasionally contained a few degenerated fibers. In the brain stem, in addition to the degeneration in the upward continuation of the ascending tracts of the spinal cord, degeneration was also found in the mesial and lateral fillets and in the ascending fibers of the dorsal longitudinal bundle. Degenerated fibers were also found in the intramedullary portions of some of the sensory cranial nerves, especially the eighth and the fifth. Generally speaking, it is the afferent side of the nervous system which is specially affected, but so far degenerative changes have been found only in the first and second neurons. All the afferent nerves of the head that were examined, the

optic nerve, the sensory fibers of the trigeminal nerve and the auditory and vestibular fibers of the acoustic nerve, suffer greatly. The motor cranial nerves usually escape, but some degeneration has occasionally been found in the oculomotor nerve. In the body the same rule holds, the degeneration affecting primarily the dorsal root fibers, the anterior roots remaining normal except when the nutritional deficiency has been very prolonged. No degeneration has been noted in the vagus nerve, even in its afferent fibers.

Mellanby investigated the changes in the nerve cells in these animals. He employs the phraseology introduced by Marinesco, i. e., primary degenerative changes as the result of toxic agents and secondary degenerations due to injury of the axon. When the lesions are primary, chromatolysis commences at the periphery of the cell and spreads toward the center, whereas in secondary or traumatic degeneration the chromatolysis begins centrally and spreads toward the periphery. In the present investigation the changes in the nerve cells can be classified among the primary or toxic group, though produced by ordinary foodstuffs without the addition of any known toxic agent. On the whole, Marinesco's generalization as to the peripheral changes in the Nissl bodies in primary degeneration applies to the present results, with some exceptions. Real chromatolysis in the sense used by Nissl is not very common and when present generally affects a small portion of the periphery of the cell or the nucleus. A few instances of chromatolysis comparable with that seen in secondary degeneration were found, more especially in certain cells of the medulla. More often the granules lose their discrete form and are in a powdery or lightly staining condition, the parapyknomorphic change of Nissl. At times the Nissl bodies may be aggregated into clumps, and in other cases they may be so changed that the cell takes on a more intense, even stain and is described as chromophilic.

SALL, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

ULTRA-VIOLET TREATMENT OF DEBILITATED CHILDREN. GEORGE H. DAY, Brit. J. Phys. Med. **10**:88 (Oct.) 1935.

Day comes to the conclusion that: "Debilitated children regain their weight more quickly if treated with ultraviolet rays than if treated with cod liver oil." The evidence is not convincing.

HARTMAN, Cleveland.

RICKETS. J. C. SPENCE, Practitioner **136**:196 (Feb.) 1936.

Spence points out that adequate calcification of the bones requires three conditions: (1) that the diet shall contain the materials to stimulate and maintain growth and also sufficient calcium and phosphorus to supply calcium salts, (2) that these materials shall be sufficiently absorbed from the bowel and (3) that the body shall be supplied with a certain "specific kind of energy" to promote and regulate calcification of growing bones.

The most satisfactory and accurate method of diagnosis is the roentgen examination of the epiphysial line of a long bone. The use of the radial epiphysis is well suited for this purpose. Clinical findings may also be of value, and the physical signs of craniotabes, beading of the ribs and enlargement of the radial epiphyses are important aids to diagnosis.

Under treatment the author notes that there are four ways in which curative agents may be supplied: (1) by correcting the diet to include more foods containing vitamin D, (2) by adding a rich source of natural vitamin, such as cod liver oil, (3) by including in the diet artificial vitamin in the form of viosterol or calciferol, and (4) by irradiating the patient's skin with sunshine or with rays of the ultraviolet lamp. The writer suggests that a diet sufficient to prevent and probably to cure rickets would be: 1½ pints (852 cc.) of milk, two egg yolks, 2 ounces (56.7 Gm.) of liver, meat or fish, butter and an average helping of fresh green salad or vegetables. In the presence of active rickets cure would be made more rapid by adding cod liver oil. It takes from ten to fifteen weeks to cure active rickets under this schedule. The author highly recommends the use of follow-up roentgenograms to estimate the state and progress of the disease.

SAPPINGTON, San Francisco.

LATE RICKETS. DONALD PATERSON, Proc. Roy. Soc. Med. **29**:213 (Jan.) 1936.

A boy of 10 years was admitted to the hospital weighing 47 pounds (21.3 Kg.) and measuring 46 inches (116.8 cm.). There were only eight teeth in each jaw. The epiphyses at the wrists, ankles and knees were enlarged, and there was slight kyphosis. Roentgenograms showed long-standing rickets and right coxa vara. The report is accompanied by roentgen pictures of the right wrist, which show typical active rickets.

WILLIAMSON, New Orleans.

RICKETS WITH UNUSUALLY LOW BLOOD CALCIUM. ALLAN MONCRIEFF, Proc. Roy. Soc. Med. **29**:214 (Jan.) 1936.

A girl of 19 months was the third child of a healthy family. Mild rickets was noted when she was 12 months old. She could stand well at 9 months, but at 17 months she could hardly sit up alone. At 19 months she had a convulsion, and one week later she was admitted to the hospital. On admission she had general atonia, a marked rickety rosary and enlarged epiphyses, and laryngismus stridulus was present on crying. The calcium content of the blood was 4.3 mg. per hundred cubic centimeters, and the inorganic phosphorus content was 3.2 mg. The results of examination of the urine and blood, the roentgenologic findings and the progress and treatment are all given in the report.

WILLIAMSON, New Orleans.

THE RÔLE OF THE VITAMINS IN OPHTHALMOLOGY. H. VIALLEFONT and E. DIACONO, Arch. d'opht. **52**:723 (Oct.) 1935.

Reference is made at this time only to the known facts concerning vitamins in relation to conditions of the eyes, and to some personal observations. Those conditions recognized as being due to a lack of vitamin A are cited, and their early diagnosis is briefly discussed. Conditions benefited by vitamin A therapy, that is, the chronic forms of keratitis, phlyctenular disease and allied conditions, are referred to, and the case of a syphilitic patient in whom an indolent, refractory ulcer of the cornea healed promptly after local instillation of an oily solution of vitamin A and cod liver oil is reported. Thus there are conditions due definitely to lack of this vitamin, conditions that are benefited by general treatment with the vitamin and conditions that are helped by local treatment with the vitamin. Some reference is made to hypervitaminosis. Vitamin C is discussed in a similar way. Absence or insufficiency of this vitamin is suggested as a possible factor in the causation of recurrent hemorrhages in the vitreous. Its relationship to the development of cataract is reviewed. From a practical point of view the authors believe that ophthalmologists should be aware of the frequency of vitamin deficiency and of the usefulness and efficiency of vitamin therapy, especially of local vitamin therapy, which is harmless and worthy of consideration in daily practice.

MARLOW, Syracuse, N. Y. [ARCH. OPHTH.]

RICKETS AND THE ULTRAVIOLET RAYS. ARVID WALLGREN, Curé Marine **5**:95, 1935.

In Sweden natural heliotherapy is not as a rule employed as the principal method of treatment of rickets. Sunlight in that latitude is too poor in ultraviolet rays and the temperature of the air is too low to allow the utilization of the natural radiation of the sun during the season of the year when rickets is prevalent. Nor is the treatment by radiation from the mercury vapor arc in quartz widely practiced, on account of chills and the danger of acquiring infectious diseases to which the child is easily exposed in the heliotherapy clinics. In Sweden the method of choice in the treatment and prophylaxis of rickets is, in addition to a well balanced diet and the usual hygienic measures, indirect application of ultraviolet rays by means of cod liver oil or irradiated ergosterol.

WALLGREN, Gothenburg, Sweden.

THE SYNTHESIS OF CEVITAMIC (ASCORBIC) ACID. G. MOURIQUAND, A. CŒUR and P. VIENNOIS, Nourrisson **24**:144 (May) 1936.

It has been shown that certain animals (rats and pigeons) are able to synthesize their own vitamin C when their diets are lacking in this factor. Other animals (guinea-pigs and human beings) do not possess this *léger d'adrénale*. On account of the infrequence of scurvy in young infants, Rohmer and Bezssonoff have raised the point that perhaps young infants possess this ability to synthesize vitamin C, though the ability is lost after the first few months. Reasoning by analogy, they conducted experiments to find out whether young guinea-pigs during the first twenty days of their lives are able to synthesize their own vitamin C. They have shown that they are not able to do so and conclude that young infants also lack the ability to make their own vitamin C.

McCLELLAND, Cleveland.

THE PROPHYLAXIS AND TREATMENT OF RICKETS. H. VIGNIS, Progrès méd., March 21, 1936, p. 488.

This is a brief article on the subject of rickets, containing nothing new.

LESLIE, Evanston, Ill.

PROPHYLAXIS OF RICKETS AND TETANY (SPASMOPHILIA). EMILE WIELAND, Rev. franç. de puériculture **3**:143, 1935.

Wieland expresses the belief that only by official regulation ordering the combination of vitamin D with the daily feeding of the infant can the needs of all infants for prophylaxis against rickets be sufficiently provided. The best procedure is considered to be the irradiation of good fresh milk and insistence that this be supplied to all artificially fed infants during the first six months of life. For breast-fed infants the daily administration of a pharmaceutic preparation of vitamin D, such as viosterol, should be required. All irradiated substances should be standardized in international (U. S. P.) units of vitamin D.

CRANE, Chicago.

RICKETS IN INFANCY. J. P. GARRAHAN and E. MUZIO, Semana méd. **2**:1805 (Dec. 13) 1934.

Garrahan and Muzio found craniotabes in a majority of their patients with rickets in Buenos Aires. However, many patients who had craniotabes did not show rickets by roentgenograms. They found craniotabes most frequently in premature and syphilitic children. They think, therefore, that the condition may not mean rickets or syphilis in some children, but that in many it does. The treatment they use for rickets is the administration of 30 drops of irradiated ergosterol a day.

SANFORD, Chicago.

THE EFFECT OF NUTRITION ON THE VITAMIN C CONTENT OF THE SPINAL FLUID AND THE POSSIBILITY OF DIAGNOSING C-HYPOVITAMINOSIS BY MEANS OF EXAMINATION OF THE SPINAL FLUID. F. PLAUT and M. BÜLOW, Ztschr. f. d. ges. Neurol. u. Psychiat. **152**:324 (March) 1935.

The average vitamin C content of the cerebrospinal fluid was determined for a series of control subjects. It varied definitely with the age of the subject; for those between 20 and 35 years of age it was 1.77 mg. per hundred cubic centimeters; for those between 36 and 59, 1.97 mg., and for those between 61 and 83, 0.51 mg. Plaut and Bülow observed progressive diminution in the vitamin C content of the spinal fluid of four patients with schizophrenia and of one mentally defective person during their residence in a hospital for patients with mental disease. In one case the vitamin C content of the spinal fluid was reduced to as little as a quarter of its first value in a few months. In the other four cases it was reduced to about 50 per cent of its original value, the reduction in one of

the cases taking place after fourteen days of hospitalization. Control studies of the spinal fluid obtained from the same patient at intervals of three days showed that such spontaneous variations were not usual.

The authors report the effect of feeding vitamin C on the vitamin C content of the spinal fluid of human beings. One hour and two and a quarter hours after 300 cc. of orange juice was given by mouth a lumbar puncture was done. No change was found in the vitamin C content of the spinal fluid. Longer periods of feeding with vitamin C were tried for seven, eight and fourteen days, 90 mg. of cevitamic acid being given daily in the form of 9 tablets. The amount of vitamin C given was the equivalent of that in about 150 cc. of lemon juice. All the persons studied had a low vitamin C content of the spinal fluid. In all a definite increase in vitamin C content was noted after prolonged feeding. A definite increase was noted after seven days and further rises after fourteen days. When the feeding was stopped, no decrease was noted for ten days. Three weeks after the cessation of the feeding the values for vitamin C were lower, but not yet normal. The authors conclude from these observations that feeding of vitamin C definitely raises the vitamin C content of the spinal fluid of human beings.

A similar relation was found in rabbits. The vitamin C content of spinal fluid of rabbits is higher in the summer than in the winter because the food eaten during the summer contains more vitamin C. In four rabbits it was demonstrated that by feeding foods containing vitamin C the amount of this vitamin in the spinal fluid could be increased. Cevitamic acid, injected intrathecally, disappeared rapidly from the spinal fluid of rabbits. After the oral administration of this acid to human beings the amount of this substance in the spinal fluid increased and did not decrease very readily. One cannot, therefore, conclude much regarding the physiologic chemistry of vitamin C in human beings from experiments on animals.

Fifty cubic centimeters of lemon juice was fed to a group of rabbits by means of a tube. Spinal puncture was performed on all before the feeding and on groups of two or three at intervals of one, two, three, four, five, six and twenty-four hours after feeding. In none of the animals was there any increase in vitamin C in the spinal fluid. In another group 100 mg. of pure cevitamic acid was injected intravenously. In these animals the vitamin C content of the spinal fluid was increased one-half hour after the injection, and an increased amount was still present twenty-four hours later. The increase was somewhat more than 1 mg. per hundred cubic centimeters.

Differences in the vitamin C content of the diets of young and old patients cannot account for the differences in the amount of vitamin C in the spinal fluid. To prove that the length of stay in the hospital of the older patients played no rôle, spinal puncture was carried out on admission on fifteen patients between 20 and 30 years of age and on fifteen between 55 and 77. The average vitamin C content of the spinal fluid of the younger patients was 2.11 mg. per hundred cubic centimeters, and that of the older patients, 0.60 mg. The length of exposure to hospital diet, therefore, cannot account for the difference in the vitamin C content between the two groups. This difference is not due to defective absorption of the vitamins in the older persons, because in three (ages 64, 74 and 72) the vitamin C content of the spinal fluid increased after the oral administration of the vitamin, just as it did in the younger patients. The conclusion is therefore justifiable that the lower values for vitamin C in the spinal fluid of older persons is due to a decreasing intensity of the metabolic processes concerned with the elaboration of vitamin C.

In instances of induced malaria, the febrile course of the disease decreases the vitamin C content of the spinal fluid.

The quantitative determination of vitamin C in the spinal fluid, considering the age of the patient and other modifying factors, such as febrile diseases, can be used as a measure of the degree of C hypovitaminosis. The quantitative determination of this vitamin in the spinal fluid is much easier than similar investigations of the vitamin content of blood or urine.

SAVITSKY, New York. [ARCH. NEUROL. & PSYCHIAT.]

PHOTOCHEMICAL AND BIOLOGIC ASSAY OF THE ULTRAVIOLET VALUE OF TSINAN SUNLIGHT. A. V. SCOTT, P. K. LI and P. C. JEN, Chinese M. J. **49**:1311 and 1315 (Dec.) 1935.

Scott, Li and Jen are in the School of Medicine, Cheeloo University, Tsinan, Shantung, China. Readings were made daily during 1932, with the acetone-methylene blue gage. In the first portion of this work the photochemical assay is reported, and two charts made at Tsinan are compared with charts published in the AMERICAN JOURNAL OF DISEASES OF CHILDREN by various observers. In the second portion, the biologic estimation is given. Daily exposure of albino rats to spring sunshine for two minutes prevented rickets; similar results occurred with summer sunshine for ten minutes, autumn sunshine for seven minutes and winter sunshine for ten minutes.

NEFF, Kansas City, Mo.

## Hygiene; Growth and Nutrition; Public Health

HEALTH PITFALLS AND TRAGEDIES OF THE PRESCHOOL CHILD. L. P. MCHAFFIE, Arch. Pediat. **53**:639 (Sept.) 1936.

The preschool period is important in the child's development. Unfortunately it is during this period that his physical welfare is apt to be overlooked and neglected. Preschool medical and dental clinics are urgently needed to continue the good work of the infant welfare stations, bridging the gap between these and the school services. McHaffie outlines the various services that should be offered by an ideal preschool clinic.

ORR, Buffalo.

GROWTH AND DEVELOPMENT WITH SPECIAL REFERENCE TO DOMESTIC ANIMALS: XXVI. THE ENERGY INCREMENT OF STANDING OVER LYING AND THE COST OF GETTING UP AND LYING DOWN IN GROWING RUMINANTS (CATTLE AND SHEEP); COMPARISON OF PULSE RATE, TIDAL AIR, AND MINUTE VOLUME OF PULMONARY VENTILATION DURING LYING AND STANDING. W. C. HALL and S. BRODY, Missouri Agric. Exper. Stat., Research Bull. 180, January, 1933.

Data are presented showing that the increments of energy in standing over that in lying are from 9 to 13 per cent. The percentage increase in the pulse rate in standing over the pulse rate in lying is from one third to one fourth of the percentage increase in oxygen consumption. The respiration rate is decreased by from 10 to 12 per cent in standing as compared with lying, but this decrease is compensated by a proportional increase in the tidal air, so that the increase in the volume of air exhaled per minute is of the same order as the increase in oxygen consumption. The pulse rate in quietly resting cattle at from eight to fourteen hours after feeding is about 69 beats per minute, being of the same order as in human beings. The respiration rate in cattle under given conditions of food supply is above 29, which is much higher than that in human beings. The tidal air in cattle varies largely with the weight of the animal, ranging from 1,400 cc. in a 4 month old calf to 4,500 cc. in a very heavy steer. The minute volume of pulmonary ventilation varies directly with the oxygen consumption and ranges from 46 liters per minute in the calf to 135 liters in the steer. During fasting, all the cardiorespiratory activities decline. The percentage decline during fasting was least for the tidal air and greatest for the rates of respiration and ventilation. The combined energy cost of getting up and lying down for medium-sized cattle is of the order of 8 calories per animal or 2.5 calories per 100 kilograms of live weight. It appears that most of this energy is expended for getting up and little of it is expended for lying down. The body weight and the pulse rate have coefficients of variation of the same order, about 10 per cent. The rates of oxygen consumption, ventilation and respiration and the value of the tidal air also have coefficients of variation of the same order, about 20 per cent, i. e., about double those for the body weight and the pulse rate.

VINTON, New York.

MEDICAL SUPERVISION OF SUMMER CAMPS. W. L. FUNKHOUSER, South. M. J. **29**:422 (April) 1936.

Three factors, fatigue, worry and insufficient sleep, are paramount causes of illness in camp, and they must be held constantly in mind by all responsible for the campers. It is incumbent on the medical officer to watch for these three factors at all times.

There are a number of problems of mental hygiene in camp. It should be the province of every camp management to supervise and correct any emotional irregularities. The mental and physical development of the camper should proceed together, with the same consideration given to the one as to the other.

Individual instruction in sex hygiene should also be given to the younger campers if their parents request it.

The principal causes of illness were found to be exposure, improper eating, sudden change in the weather, fatigue and emotional strain.

SCHLUTZ, Chicago.

RECENT METHODS IN THE PREVENTION OF DISEASE: CRITICAL REVIEW. A. B. SCHWARTZ, Wisconsin M. J. **34**:911 (Dec.) 1935.

To be successful methods of preventive immunization must withstand the critical tests of every laboratory, hospital and private physician.

Records of revaccination against smallpox indicate that a high percentage of those who have had a successful vaccination remain protected for many years; so repeating vaccination every seven years is superfluous in most cases. The initial vaccination is better done in the last half of the first year of life than in the first half.

Mortality rates for diphtheria have dropped in the urban population from 13.13 per 100,000 of population in 1923 to 2.23 in 1934. The rates for comparable English and German groups have dropped less rapidly, those in 1933 being 8 and 8.2, respectively. Eradication depends on immunization of the preschool child. Alum-precipitated toxoid administered in one or two doses is advisable for those under 6 years of age; for those over 6 years and for adults not immune, three doses of potent toxin-antitoxin two weeks apart followed by a Schick test in six months is recommended.

Convalescent human serum is well established in the prevention and modification of measles. Placental extract (immune globulin), while generally reported on favorably, causes marked local and general reactions in many instances and also is less efficient.

Sauer's vaccine for active immunization against pertussis has proved satisfactory, giving protection in 93 per cent of a goodly series of cases.

The questions of the value both of serum in the prophylaxis and treatment of poliomyelitis and of active immunization by other methods are still unsettled.

The immunization against scarlet fever, while subject to certain objections, is becoming increasingly more used, and statistics confirm its value. The favorable results obtained by the use of convalescent scarlet fever serum show its value both as a temporary protection for those exposed and as a valuable therapeutic aid for those who are ill. The complications of scarlet fever are materially reduced by the use of the serum.

The BCG vaccine as a control for tuberculosis, favorably reported on by some, is warned against by others.

Hoyne gives a favorable report on the Ferry antitoxin in the treatment of meningococcic meningitis.

JANNEY, Wauwatosa, Wis.

MORTALITY FROM GASTRO-ENTERITIS IN THE CHILD UNDER TWO YEARS OF AGE IN FRANCE AND IN SOME FOREIGN COUNTRIES. MOINE and LECLAINCHE, J. de méd. de Paris **55**:1091 (Dec. 12) 1935.

This is a statistical study which cannot well be abstracted. The statistics for the infant mortality from gastro-enteritis in France, Belgium, Switzerland, Spain, England, Japan, Uruguay and Massachusetts from the years 1910 to 1930 are analyzed.

LESLIE, Evanston, Ill.

NORMAL GROWTH AND ITS VERIFICATION. B. WEILL-HALLÉ, Rev. franç. de puériculture **3**:193, 1935.

Weil-Hallé discusses the various standards proposed for the determination of normal growth. He emphasizes that these are all approximations and that the individual growth curve and the findings on physical examination are of greater importance.

CRANE, Chicago.

MEASUREMENTS OF HEIGHT, WEIGHT AND CHEST CIRCUMFERENCE IN CHILDREN IN ADOLESCENCE. W. KORNFELD, Ztschr. f. Kinderh. **55**:720, 1933.

Kornfeld believes that the measurements of height, weight and chest circumference in children in adolescence as given by Schlesinger are too low. He refers to his own and to the Pirquet-Camerer figures.

LEVINSON, Chicago.

## Prematurity and Congenital Deformities

HARE-LIP. H. DOUGLAS STEPHENS, Brit. M. J. **1**:5 (Jan 4) 1936.

Stephens presents an outline of the subject of hare-lip, with suggestions as to the age for operation, the feeding of the infant, the preoperative management, the operation itself, the technic for which is described, and the postoperative care.

ROYSTER, University, Va.

CRANIOFACIAL DYSOSTOSIS (CROUZON'S DISEASE). F. MÉDINGER and G. MORARD, Arch. d'opht. **52**:489 (July) 1935.

This condition is characterized by: (1) deformities of the skull; (2) facial deformities involving the nose, orbit and superior maxilla, giving rise to prognathism of the lower jaw; (3) ocular involvement, such as exophthalmos, divergent strabismus, nystagmus and lesions of the optic nerve producing blindness; (4) hereditary and familial traits. Médinger and Morard have been able to collect eighty-three reports from the literature. Sixty-nine cases which they were able to trace occurred in thirty-nine families; forty-six were familial, twenty-three solitary. They describe a personal observation in detail. In discussing the ophthalmic symptoms they point out that exophthalmos is always present, though of varying degree. The condition is never accompanied with trophic disturbances of the cornea due to pressure on the ciliary ganglion, or with intrinsic paralysis of muscles or with high hyperopia. It is frequently accompanied with widening of the interorbital space. Divergent strabismus was present in thirty of sixty cases. Nystagmus has been observed and is probably associated with defective vision. Among sixty patients, atrophy of the optic nerve was complete in fifteen and partial in eighteen; in the remaining thirty-seven the optic nerve was normal. The development of atrophy of the optic nerve is slow and progressive and has been found at various stages of the disease. No treatment other than the possible prevention of the occurrence of the disease is effective. A full bibliography is appended.

MARLOW, Syracuse, N. Y. [ARCH. OPHTH.]

SACROCOCCYGEAL AGENESIA. J. A. SOTO and M. PLACE, Arch. de pediat. d. Uruguay **7**:366 (Aug.) 1936.

This condition occurred in a child aged 1½ years. There was some rigidity of the extremities. A kyphosis with an osseous consistency was present in the lumbar region. The sacrum was not felt; intergluteal folds and prominence of the buttocks were absent; there was flattening of the region in which the anal orifice opened. Incontinence of urine and feces was present. The x-ray photo-

graph showed that the vertebral column terminated at the level of the fifth lumbar vertebra, below which there was a small osseous body which might represent a rudimentary sacrum. The sacrum and coccyx were absent. There was marked hypoplasia of the twelfth dorsal and first lumbar vertebrae, giving rise to lordosis at this level and to kyphotic prominence of the first vertebra below. The iliac bones closely approached each other, with corresponding narrowing of the pelvis. There were bilateral dislocation of the hips and bifurcation of the twelfth rib at its posterior end. There were bilteral inguinal hernia and umbilical hernia. There were no changes in the long bones or periosteum and no abnormality of the heart and lungs. The Wassermann reaction was negative, and there was no history of consanguinity.

SCHLUTZ, Chicago.

COMMENTS ON A CASE OF CONGENITAL EQUINOVARUS. L. RIBO RIUS, Paidoterapia **13**:687 (Oct.) 1934.

A single instance of bilateral congenital equinovarus is reported, and a short discussion of the subject is given.

HERRON, Spokane, Wash.

PHYSIOLOGIC FETAL MALPOSITION. FELIX BAUER, Wien. klin. Wchnschr. **48**:1352 (Nov. 1) 1935.

Until recently it was believed that even under normal conditions the position of the fetus may be somewhat cramped. There is now a tendency to regard fetal malposition as pathologic. To solve the problem of whether or not there may be physiologic fetal malposition Felix Bauer made clinical examinations of hundreds of infants. He found that in 7 or 8 per cent of the infants there is a disposition to lie on one side, the right more often than the left. There is energetic resistance to any attempt to change this position by force, and the favorite position is reassumed. The tendency to lie on one side may be connected with the following malformations, which the author believes may frequently be due to physiologic fetal malposition: wryneck, congenital dislocation of the hip and, less frequently, clubfoot, talipes and calcaneous or rachitic scoliosis.

The three forms of congenital wryneck may be listed as follows: (1) those without change in the muscle—habitual contracture; (2) those in which the muscle is stretched—long, persistent contracture, which is accentuated toward the end of pregnancy; (3) pathologic changes—birth injuries. The disposition to wryneck is to be found not in hereditary inferiority but in previous persistent fetal malposition. In fourteen cases of congenital dislocation of the hip Bauer was able to show clearly a relation to fetal malposition. Toward the end of the first year six of the infants showed, in addition, asymmetry of the skull and differences in the folds of the thigh.

ABT, Chicago.

LEVULOSE AND GALACTOSE TOLERANCE IN PREMATURELY BORN INFANTS. W. FABISCH and F. ETZOLD, Ztschr. f. Kinderh. **55**:702, 1933.

Fabisch and Etzold studied the urine of premature infants after feeding them large amounts of levulose and galactose, with the hope of ascertaining their tolerance for these two substances.

They found an average galactose tolerance of 1.6 Gm. and a levulose tolerance of 1.5 Gm. per kilogram of body weight. This compared with a galactose tolerance of 2.2 Gm. and a levulose tolerance of 2.6 Gm. in full term babies.

They came to the conclusion that the liver of the mature infant utilizes more levulose than galactose, while the liver of the premature infant utilizes more galactose than levulose.

LEVINSON, Chicago.

HEREDITY OF SUBMUCOUS CLEFT PALATE. H. MAHLSTEDT, Ztschr. f. Laryng., Rhin., Otol. (Teil 1: Folia oto-laryng.) **26**:347 (Nov.) 1935.

Mahlstedt designates rhinolalia aperta as the classic symptom of the submucous cleft palate. Depending on the size of the defect, the symptom is more or less

severe. Examination of a patient with this symptom, particularly if the soft palate is raised, discloses in the hard palate a smaller or larger wedge-shaped defect which is covered with membrane. The uvula may be absent; there may be uvula bifida, or the uvula may be intact. It has been suggested that the submucous cleft palate represents incomplete spontaneous repair of the total cleft palate. Familial occurrence of the deformity indicates that it is a hereditary defect. The cases which are described by the author are of interest because the condition appeared in three successive generations. The diagram of the genealogical tree of this family indicates that the defect was transmitted to all members (two boys and one girl) of the first filial generation by a defective father in union with a normal woman. Two members of this filial generation (one brother and the sister) married healthy persons, and the defect appeared in three of five children in the one family and in two of three in the other. In all these persons with submucous cleft palate the uvula was missing, but the cleft in the palate differed in size. The author emphasizes that the defect was more severe in the family of the brother than in that of the sister. He points out, further, that submucous cleft palate, harelip and total cleft palate differ only in degree and that for this reason it is advisable to record the cases of submucous cleft palate in the genealogical trees of families in which such defects occur, even if the submucous defect is only slight. The author thinks that if this is done many of the genealogical trees will look quite different, and he hopes that more light will be thrown on the mode of hereditary transmission, so that it may eventually be decided whether the transmission is dominant or recessive.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

## New-Born

THE SURGICAL TREATMENT OF CONGENITAL TRACHEO-ESOPHAGEAL FISTULA IN THE NEW BORN. MIMS GAGE and ALTON OCHSNER, Ann. Surg. **103**:725 (May) 1936.

While congenital malformation of the esophagus is not common, the authors believe that as one becomes familiar with the clinical manifestations, the incidence of reported cases will increase.

The symptoms of esophageal atresia and tracheo-esophageal fistula are so constant that the lesion should be easily recognized. The symptoms can be divided into two main groups, (1) gastro-intestinal and (2) pulmonary. The infant at birth is well developed and appears normal except for an excessive amount of mucus in the mouth. At times the secretion is so abundant that it interferes with breathing, and attacks of cyanosis occur. These symptoms result from the filling and emptying of the blind pouch of the proximal segment of the esophagus. The abdomen rapidly becomes distended by the ingress of large quantities of air from the trachea through the fistula into the stomach and small intestine.

The classic symptoms are referable to the pulmonary system and occur dramatically at each feeding. On the first attempts at feeding nothing happens for a few seconds, but soon a definite train of events occur. There is a cough; fluid, which is often frothy, is regurgitated through the mouth and nose, and early cyanosis occurs. Almost lifeless relaxation occurs; the cyanosis disappears, and the infant recovers, to go through an identical process at the next feeding.

If a new-born infant has an excessive flow of mucus from the mouth and the abdomen rapidly becomes distended (a valuable diagnostic sign, according to Brennemann), the upper part of the esophagus should be immediately investigated. A catheter should be passed into the esophagus, and if an obstruction is met one can almost with certainty diagnose the presence of esophageal atresia. Then iodized poppy-seed oil 10 per cent should be injected into the esophagus and a roentgenogram taken.

The treatment is entirely surgical. Two definite surgical procedures are indicated: (1) closure of the fistula and (2) the opening of an avenue (gastrostomy) through which the infant can be nourished. The present mortality is 100 per cent.

BANTIN, Omaha.

DELIVERY BY CESAREAN SECTION OF AN INFANT WEIGHING 2,700 GM. FROM A FIBROID UTERUS WEIGHING 5,400 GM., WITH SURVIVAL OF MOTHER AND CHILD. P. BRAULT and A. MOISAN, Bull. Soc. d'obst. et de gynéc. **24**:440 (July) 1935.

A woman 38 years of age had been married ten years and had a miscarriage after several weeks of pregnancy in the second year of her married life. There had been no other pregnancies until the one reported here. When she was examined about a month before term, a large abdominal mass was found extending almost to the xiphoid process. The surface was irregular and firm. The fetal parts could not be felt. The fetal heart tones could easily be heard. A roentgenogram showed a well developed fetus lying transversely, with the head in the right iliac fossa and the buttocks in the left. There were no fetal parts in the minor pelvis. In about a month labor pains began, the membranes ruptured and meconium was passed. With the mother under spinal anesthesia a low cesarean section was done, and a living girl was delivered. This was followed by a subtotal hysterectomy. The uterus, which contained numerous large fibroid tumors, weighed 5,400 Gm., exactly twice the weight of the child. The postoperative course was uneventful except for a mild phlebitis. Fifteen months later the mother and the child were in normal health.

GLASER, Rochester, N. Y.

RUPTURE OF THE ROOTS OF THE BRACHIAL PLEXUS IN TRAUMATIC RADICULO-FUNICULO-PLEXITIS. V. CHOROSCHKO, Encéphale **30**:126, 1935.

Six cases of posttraumatic paralysis of the brachial plexus are reported, diagnostic tests with iodized poppy-seed oil 40 per cent being carried out with the patient lying on his side. The trauma was always severe and involved the roots of the nerves. In one case the transit of the iodized oil was normal. In spite of complete paralysis of the upper limb, with muscular atrophy, enophthalmia, etc., a favorable prognosis was given and "confirmed by later observation," of which no detail is given. In the five other cases the iodized oil was arrested at the level of the different cervical nerve roots on the affected side (the seventh in three cases, the fifth and sixth in one case and the eighth in one case) and formed large rounded drops which protruded beyond the limits of the dura. The conclusion was that the corresponding roots were ruptured at or near their emergence from the dura. In none of these cases was there any notable improvement during periods of observation varying from four months to over a year. In two cases iodized oil seemed to fill a cavity or cyst when the patient was lying on his side, but reentered the dura and fell freely to the bottom of the sac when the patient sat up. In one of these cases laminectomy showed an oval extradural cyst, containing clear fluid. Intradural radicular rupture is more frequent than most clinicians believe. The diagnosis and localization can be asserted only after examination with iodized oil.

LIBER, New York. [ARCH. NEUROL. & PSYCHIAT.]

CONGENITAL PEMPHIGUS. WILLEMIN-CLOG, STOERR and CARDYN, Nourrisson **23**: 243 (July) 1935.

A case of bullous dermatitis is described in which the lesions were present at birth and persisted up to the time of reporting, when the baby was 5 months old. The mucous membranes of the mouth and tongue were also involved. The baby was poorly nourished and had numerous bouts of fever. The serologic reactions were negative for syphilis. Bacteriologic studies did not disclose any etiologic micro-organism. No successful treatment was discovered. Exposure to the ultraviolet rays had an unfavorable effect.

MCCLELLAND, Cleveland.

CEREBRAL-MENINGEAL LESIONS OF THE NEW-BORN: CLINICAL CONSIDERATIONS AND ANATOMICOPATHOLOGIC RESIDUALS. P. BRUSA and N. ORLANI, Riv. di clin. pediat. **34**:1 (Jan.) 1936.

Six cases of intracranial hemorrhage in new-born children are reported. One child died within thirty-six hours after birth, four others within fifteen days and

one within six and one-half months. Brusa and Orlandi emphasize that intracranial hemorrhage of a severe nature may occur without marked obstetric trauma. They further emphasize that the symptoms of intracranial hemorrhage may be suppressed during the first days of life. Whereas hyperthermia in some new-born infants may be a manifestation of iintracranial hemorrhage, in others hypothermia may also be a striking symptom; in other words, the bulbar and medullary centers as well as the higher functions of the brain may demonstrate either overactivity or inhibition. The pathologic effects of the cerebromeningeal hemorrhage are illustrated by photographs of sections of brains and meninges obtained at necropsy.

HIGGINS, Boston.

SEVERE INTRACRANIAL HEMORRHAGE IN DELIVERIES FREE FROM COMPLICATIONS AND IN CESAREAN SECTION. ALEXANDER EBERGÉNYI, Jahrb. f. Kinderh. **144**: 291 (May) 1935.

Three cases of births free from complications in all of which there was severe intracranial bleeding are reported.

The first case is that of a 3,800 Gm. child delivered easily, in which the signs of intracranial bleeding included the following: cyanosis, hematomas under the integument of the upper and lower eyelids, somnolence, convulsions and periods of asphyxia. These gradually cleared up, but the child was obviously an idiot. The mental condition improved gradually with the signs of resorption of the blood, giving evidence to the idea that the idiocy was a direct result of the intracranial bleeding. Death followed gastro-enteritis. An autopsy was not done. Heightened tissue fragility was considered to be the cause of the bleeding in this case. The clotting time, bleeding time and blood picture were normal.

The second case is that of a child of a 45 year old primipara. Delivery was by cesarean section because of the development of signs of renal insufficiency. This child died within an hour. At postmortem examination a tentorial tear was found. The tentorium was thinner than normal. The condition was ascribed to increased tissue friability, which may have been influenced by the kidney condition of the mother.

In the third case, a 5,000 Gm. giant, the child of a quadripara, aged 38, died in utero. Three previous children had died within a few days of birth or were born dead as the result of intracranial bleeding. All were very large children. At postmortem examination a torn vein was observed to be the source of the bleeding. Abnormal tissue friability is considered to be the etiologic factor in this case also.

Recently it has been emphasized that the asphyxia seen in new-born children is to be explained not on the basis of compression but as a caisson-like effect, or decompression. This may account in part for the origin of intracranial bleeding through pressure on the promontory of the skull, especially in infants with abnormal tissue friability, the bleeding following the release of pressure.

LANDAU, Rochester, N. Y.

USE OF CORAMINE IN ASPHYXIA NEONATORUM. R. HOME, München. med. Wchnschr. **82**:823 (May 23) 1935.

Home treated twenty-one infants with asphyxia neonatorum with injections of a cardiac stimulant. Fifteen were given intramuscular injections of from 1 to 2 cc.; six were given from 0.5 to 1 cc. injected into the vein of the umbilical cord. The drug is best injected into the umbilical vein before the cord is tied. If there is doubt as to the necessity for stimulation before the cord is tied, it can be left long enough to permit an injection a short time later. The results of the treatment were surprising and striking. Immediately following the intravenous injection the breathing became deeper and, in a short time, regular. Cardiac stimulation

also occurred, a point especially noticeable in several infants with weak heart action. One infant with severe asphyxia who died was shown at autopsy to have a cerebral hemorrhage.

BRAHDY, Mount Vernon, N. Y.

CONGENITAL SARCOMA. E. KUBÁNYI, Orvosi hetil. **79**:1025 (Sept. 21) 1935.

A 9 year old infant was operated on for a large tumor under the left arm pit. The tumor had grown quickly immediately after birth so that its weight was 112 Gm. at the time of the operation. The microscopic examination showed fibrosarcoma.

GÖTTCHE, Budapest, Hungary.

INFLUENCE OF PROTRACTED OR COMPLICATED DELIVERY ON THE OCCURRENCE OF "TRANSITORY" FEVER IN THE NEW-BORN INFANT. T. SALMI, Acta pædiat. **17**:469, 1935.

The article opens with a comprehensive survey of the numerous theories which have been elaborated to explain the occurrence of the transient fever so commonly observed in new-born infants. The various hypotheses may be resolved into five principal points. These are: (1) dehydration with all its physiologic implications, (2) infection, (3) trauma during birth, (4) the influence of the temperature of the environment and (5) the combined effect of two or more of these factors.

Salmi studied the temperature curve of 324 new-born infants. Of the 225 who were born by normal delivery, 20 per cent exhibited transitory fever. Fifty-four infants were born by cesarean section; 25 per cent of these had fever during the neonatal period. Forceps were used in delivering 45 infants; the incidence of fever in this group was 50 per cent. Critical scrutiny of the obstetric records demonstrated that, in general, the time required for delivery was of significantly longer duration in the case of the infants in whom transitory fever developed than in those who remained afebrile. This finding suggests the conclusion that the increased liability to infection and trauma at birth resulting from difficult, protracted and complicated delivery may play the principal rôle in the occurrence of transitory fever in the new-born infant.

MCCUNE, New York.

ANEMIA IN THE NEW-BORN. E. MANNHEIMER, Acta pædiat. **18**:237, 1935.

The first case reported as an instance of anemia of the new-born was that of Ecklin, in 1919. Since that time between twenty-five and thirty cases have been reported. The syndrome exhibits the following distinguishing features: (1) the presence of anemia, usually of severe degree, which is manifest at birth or shortly thereafter; (2) the presence in the circulating blood of many immature forms of both the erythrocytic and leukocytic series; (3) the absence of demonstrable cause of the hematologic abnormalities. The author states that, with the exception of the opinions held by Blackfan, Diamond and Baty and by Péhu and his collaborators, this type of anemia in the newly born is generally considered to be well delimited from congenital hydrops with erythroblastosis and from the anemia which is characteristic of icterus familiaris gravis.

On the basis of the supposition that the syndrome is a disease sui generis, several names have been proposed: *primäre Anämie des Neugeborenen* (Stransky), congenital anemia (McClelland, Pasachoff and Wilson) and anemia pseudoleukaemica neonati (Hotz). However, it is extremely doubtful whether the clinical manifestations of the disease are at all uniform. For example, there is lack of agreement concerning the occurrence of icterus, enlargement of the liver and spleen and the degree of leukocytosis. Even in Ecklin's case, a sister of the patient had died of icterus familiaris gravis; naturally this casts doubt on the correctness of classifying the condition as congenital anemia. The outcome was favorable in the majority of the reported cases, although death occurred in five. Iron, blood transfusions, injections of blood intraperitoneally and subcutaneously

and, in one case, intramuscular injection of a preparation of liver have been employed therapeutically. Restoration of health was more rapid if treatment was given, the time required for recovery varying between two months and one year. Pathologic examination of the infants who died has been disappointing. Aside from anemia, hemosiderosis, enlargement of the liver and spleen and evidence of formation of blood shown by the liver, spleen, bone marrow, kidneys, lungs, pancreas, adrenal glands and lymph glands, little has been found which casts light on the pathogenesis of the condition. Leukemia and infection have been suggested as etiologic agents.

A case of congenital anemia is reported which occurred in a white boy, the fourth in a family of constitutionally inferior children. The mother was strong, healthy and free from syphilis. The only complication of pregnancy was moderate hydramnios. The infant was born at term and weighed 3,760 Gm. He was strikingly pale at birth and exhibited over the surface of his body blue-gray spots about 1 cm. in diameter; otherwise he seemed strong and vigorous. Fifteen cubic centimeters of maternal blood was given intramuscularly, without benefit. On the eleventh day of life the infant continued to exhibit pallor and a moderate amount of purpura; in addition, the spleen and the liver extended to the umbilicus. Hematologic examination on the third day of life revealed the concentration of hemoglobin to be 66 per cent; erythrocytes, 3,200,000 per cubic millimeter, and leukocytes, 16,400 per cubic millimeter. On the eleventh day the concentration of hemoglobin was 26 per cent, and there were 1,010,000 erythrocytes per cubic millimeter; the leukocytes reached a maximum of 63,800 on the thirteenth day. At that time a large number of immature erythrocytes and leukocytes were present. The Wassermann reaction of the blood was negative; the sedimentation rate of the erythrocytes was accelerated; the platelets were not diminished, nor were the bleeding and clotting times prolonged, and a transient increase in reticulocytosis was noted. Histologic examination of a specimen of bone marrow on the twelfth day of life indicated a remarkable increase in hematopoietic activity.

The infant was treated with intraperitoneal injections of whole blood in quantities varying between 55 and 65 cc. Iron, copper and a concentrated preparation of liver were also employed. The patient's weight increased uninterruptedly; purpura disappeared promptly; the liver and spleen slowly regained their normal size. At no time was either jaundice or edema evident. At the end of the first month abnormal cells were no longer conspicuous in the stained preparations of blood; the anemia had disappeared by the time the infant was 4 months old.

The etiology in this case is obscure. Mannheimer regards the clinical picture as the result of a reaction on the part of the fetus to unknown morbid processes which affect it during pregnancy. Erythroblastosis is a primitive form of reaction to severe anemia; its occurrence in congenital hydrops and in icterus familiaris gravis does not constitute good evidence that these two conditions are causally identical with or even allied to congenital anemia. McCune, New York.

## Acute Contagious Diseases

Mumps Orchitis. Alfred Stengel, Am. J. M. Sc. **191**:340 (March) 1936.

This comprehensive, interesting article is best abstracted by presenting the author's conclusions:

"1. Mumps is caused by a virus.

"2. Orchitis in mumps is important because of the possibility of subsequent sterility or impotence.

"3. There is a definite relation between the parotid gland and the genitals.

"4. Orchitis usually follows parotitis and is more often unilateral than bilateral.

"5. Orchitis is probably a hematogenous metastasis.

"6. Orchitis is most frequent at the age of puberty; its incidence in a large number of cases is about 18.2 per cent.

"7. Rise in temperature; swelling, tenderness, pain in the testicle; subsidence of fever by lysis; later variability in size of the gland are prominent symptoms of orchitis.

"8. Orchitis may be complicated by a number of conditions, among which may be included: *a*, Meningitis and other central nervous system involvements; *b*, "atrophy" of the testis occurs in 40 to 60 per cent; *c*, impotence and sterility certainly do occur.

"9. The lesion in orchitis is probably a parenchymatous sclerosis.

"10. Diagnosis in epidemics is easy; it may be difficult in the absence of an epidemic or of marked parotitis.

"11. Prophylaxis is by prevention of the disease; treatment is purely symptomatic.

"12. The use of convalescent serum or surgical incision may give good results."

HENSKE, Omaha.

SIX NEW CASES OF CHAGAS' DISEASE IN PANAMA, WITH A REVIEW OF PREVIOUS CASES. C. M. JOHNSON and G. T. DERIVAS, Am. J. Trop. Med. **16**:47 (Jan.) 1936.

Johnson and DeRivas briefly review the literature on Chagas' disease and report six new cases with autopsy observations in two. The symptoms of the disease appear to be vague and indefinite, in contrast to those described by Chagas.

They inoculated experimental animals, with positive results. They also found that Trypanosoma Cruzi is infectious for a number of wild and domestic animals as well as man. Triatoma geniculata, Rhodnius pallescens and Eratyrus cuspidatus are insect vectors. These vectors show promiscuous tendencies, being equally partial to infants and armadillos.

They concluded that the disease is probably more prevalent in Panama than it has been thought to be and that there is probably a wider distribution of it than has been supposed. The mortality is high for infants but low for adults.

BUSPEE, Augusta, Ga.

THE EPIDEMIC OF ACUTE POLIOMYELITIS IN 1935. H. R. LITCHFIELD and B. B. COHEN, Arch. Pediat. **53**:63 (Jan.) 1936.

Not abstracted. WADDELL, University, Va.

MENINGOCOCCIC MENINGITIS: IMPORTANCE OF INTRAVENOUS THERAPY. ARCHIBALD L. HOYNE, Illinois M. J. **68**:307 (Oct.) 1935.

Hoyne states that a meningococcic invasion should be considered as a general infection due to the meningococcus and that when meningitis develops it should be looked on as a complication due to a localization of the infection. His hypothesis is based on the observation and treatment of approximately 2,500 patients during a period of years.

Instead of attacking the complication at its site (meninges) only, the author expresses the belief that treatment should be directed also against a systemic disease. He points out that the results following the use of antibacterial serum have been disappointing. He expresses the belief that the value of the commercial antiserums is due to whatever amount of toxin they may contain. His use of the antitoxin has markedly lowered the mortality figures at the Cook County Hospital.

Hoyne believes the intravenous route of administration to be essential. Complications among patients treated with antitoxin have been few, and recovery is usually prompt. He expresses the belief that the customary high rates of mortality for meningococcic meningitis can be greatly reduced by intravenous therapy and feels that eventually intraspinal administration may prove to be unnecessary.

BARBOUR, Peoria, Ill.

THE IMPORTANCE OF INTRADERMIC REACTIONS. C. A. EARLE, Illinois M. J. **68**:345 (Oct.) 1935.

In this article Earle reviews the present knowledge of the clinical use of cutaneous reactions. He discusses particularly the Schick test, the Dick test, the Pirquet test and tests for undulant fever, lymphogranuloma and allergic sensitivity. He also expresses the belief that intradermal reactions are of diagnostic value in certain cutaneous infections.

BARBOUR, Peoria, Ill.

A STUDY OF THE VIRULENCE OF MENINGOCOCCUS STRAINS AND OF THE PROTECTIVE ACTIVITY OF ANTIMENINGOCOCCUS SERA. SOPHIA M. COHEN, J. Immunol. **30**:203 (Feb.) 1936.

The virulence of a large number of stock and freshly isolated strains of meningococci was studied. Virulence was determined by the inoculation of mice with organisms suspended in gastric mucin. Marked differences were observed among both stock and recently isolated strains.

Comparative tests were made by the use of various serums in protection experiments. Wide variation in the protective activity of these serums was noted.

FOTHERGILL, Boston.

MECHANISM OF IMMUNITY IN EXPERIMENTAL POLIOMYELITIS. CLAUS W. JUNGEBLUT, J. Infect. Dis. **58**:150 (March-April) 1936.

The author's conclusions are as follows:

"The occurrence of virucidal antibodies in the serum of monkeys convalescing from a paralytic attack of poliomyelitis is very irregular with respect to the formation of such substances, the speed of their development and their maintenance over long periods of time.

"Monkeys convalescing from a paralytic attack of poliomyelitis are uniformly insusceptible to intracerebral reinoculation with the same strain of poliomyelitis virus, irrespective of whether the serum does or does not contain a demonstrable virucidal titer at the time of reinoculation.

"Monkeys which passed through a febrile cycle but have failed to develop manifest paralysis following intracerebral injection of poliomyelitis virus in combination with certain inactivating agents are fully susceptible to intracerebral reintroduction of the virus.

"Monkeys convalescing from a paralytic attack of poliomyelitis whose serum is tested before and after reinoculation fail to show any evidence of an increase in the serological titer of virucidal substances following reintroduction of the virus into the central nervous system.

"These data are discussed in their relation to the mechanism of acquired immunity in the experimental infection and to the epidemiology of the human disease."

TOOMEY, Cleveland.

TREATMENT OF MENINGOCOCCIC MENINGITIS WITHOUT INTRASPINAL THERAPY. A. U. HOYNE, Nebraska M. J. **21**:321 (Sept.) 1936.

The question is raised whether meningococcic meningitis is not a complication of meningococcic invasion of the blood stream. From that standpoint the author reasoned that it is more logical to direct treatment by antitoxin or serum into the blood stream than intraspinally. The mortality statistics presented confirm an opinion that a lower mortality results by that method. For instance, among thirty-six patients who were 20 years old or less and were treated by the intravenous route, there was only one death, or a mortality rate of 2.6 per cent. The duration of the disease was apparently much shorter. Frequent lumbar punctures were not necessary, and in some cases punctures were not even made, the diagnosis resting on positive blood cultures. Complications were found to be few. A large dose of antitoxin, for instance, from 50,000 to 100,000 units or more, was given.

HAMILTON, Omaha.

SYMPTOMATOLOGY AND TREATMENT OF ACUTE POLIOMYELITIS. JOSEPHINE B. NEAL, New York State J. Med. **35**:811 (Aug. 15) 1935.

Neal gives part of a symposium on poliomyelitis. Since Brodie has shown that the poliomyelitis virus travels from the nasopharynx through the olfactory nerve to the central nervous system, the disease must be considered as essentially of the central nervous system and not as a general disease. The initial symptoms are much the same in all forms of the disease and may be equally severe in the paralytic and the nonparalytic types. Three types of onset are noted: (1) In a small number of cases paralysis develops without premonitory symptoms; (2) another small group shows a period of remission in the development of the disease; (3) in the largest group the symptoms progress rapidly and uninterruptedly. The following symptoms are important in the early recognition of the disease. Hyperesthesia develops early and is general, especially over the spinal column and the large nerve trunks. Pain is an almost constant symptom, as is headache. Pain may be present in the neck, back, abdomen or extremities. Drowsiness alternating with irritability when the child is disturbed is a valuable sign. The mind is clear, delirium and convulsions being rare in poliomyelitis. Tremors or twitching of groups of muscles may be seen early in the disease. Cervical rigidity and a moderate Kernig, Brudzinski or Macewen sign may be present.

Neal feels that convalescent serum has no therapeutic value. Kramer's experiments on monkeys showed that lesions appeared in the anterior horns of the spinal cord before clinical symptoms developed. Lumbar puncture for reduction of intracranial pressure is of value in treatment. Absolute rest and early orthopedic consultations are advised.

AIKMAN, Rochester, N. Y.

MUMPS MENINGITIS AND MENINGOENCEPHALITIS. L. HOWARD SMITH, Northwest Med. **34**:375 (Oct.) 1935.

Smith reports six cases of meningitis and meningo-encephalitis following mumps. He also cites nine cases in which the attack occurred during an epidemic of poliomyelitis in which this disease was suspected but in which mumps had recently occurred. Five of the six patients showed complete recovery; one was left with some spasticity of one arm. The disease affected males in the proportion of 13:2 in this series, and in forty-four cases from the literature the proportion was 81.8:18.2.

SCOTT, Philadelphia.

ACUTE POLIOMYELITIS AMONG CHILDREN IN THE VICINITY OF SPOKANE IN 1934. E. J. BARNETT and C. L. LYON, Northwest Med. **34**:429 (Nov.) 1935.

From May to November 1934 there were reported from the vicinity of Spokane, Wash., one hundred and sixty-one cases of poliomyelitis, with nine deaths. One hundred and nineteen of the patients were under 15. Forty-four were under personal supervision of the authors. There was no instance of acute poliomyelitis following tonsillectomy as there had been in previous years. One death occurred in the forty-four cases; the disease in this instance was of a bulbar and meningitic type. The peak of the epidemic was in August, while in California the peak was in June of the same year. In less than half the cases the condition was abortive or nonparalytic. A normal spinal fluid was found in only one case. Three times as many boys were affected as girls; this contrasts with the usual ratio of 1.3:1. Most of the patients were between 5 and 10 years old. Of twenty-nine patients given convalescent serum in the preparalytic stage, only one had severe permanent paralysis. Sixty-one well children who were intimately exposed and given no serum did not contract the disease.

SCOTT, Philadelphia.

Cold Urticaria Following Chickenpox. Bertrand T. Fitzmaurice, Northwest Med. **34**:443 (Nov.) 1935.

A boy of 12 years acquired chickenpox. After this illness wheals developed over his body when he was exposed to cold air or to cold water. On eating ice cream his lips would swell and his throat tighten. His father had angioneurotic edema.

Scott, Philadelphia.

Summary of Current Prevalence of Communicable Diseases. Pub. Health Rep. **51**:1027 (July 31) 1936.

In the four week period from June 14 to July 11, 134 cases of poliomyelitis were reported in Alabama. The outbreak involved ten counties in the northwestern part of the state and spread into three counties in Tennessee. No increase in incidence has been reported from other sections of the country. Meningitis, scarlet fever, diphtheria and influenza showed a decrease in incidence. Smallpox totaled 534 cases, which is high. The increase was confined to the north central and mountain regions. There were 1,240 cases of typhoid, which represent an expected seasonal rise. The death rate from all causes was 11 per thousand, which is slightly higher than that in preceding years.

Sanford, Chicago.

Summary of Current Prevalence of Communicable Diseases. Pub. Health Rep. **51**:1183 (Aug. 28) 1936.

In the period from July 12 to Aug. 8, 1936, 515 cases of poliomyelitis were reported. More than one half of these cases occurred in Alabama, Tennessee, Mississippi and Kentucky. No other region reported more than the usual expected increase. Scarlet fever, measles, diphtheria, smallpox, meningitis and influenza declined. There were 2,058 cases of typhoid; the increase is an expected seasonal rise and is the lowest for the last eight years. The death rate from all causes was 11.9 per thousand, which is about the same as that in preceding years.

Sanford, Chicago.

Report of the 1935 Epidemic of Acute Anterior Poliomyelitis. K. K. Gregory, Rhode Island M. J. **19**:47 (April) 1936.

Two hundred and twenty-eight patients were cared for at the Charles V. Chapin Hospital, with a mortality of 7.1 per cent. Seventy patients were admitted in the preparalytic stage; of these, 18 subsequently acquired paralysis, of whom 2 died; 52 remained unaffected. Forty-two of the 228 showed evidence of injury to the vital centers; 15 of this group died, 5 with the ascending type of paralysis and 10 with primary bulbar involvement. The respirator was of little value in the cases of bulbar involvement but was a life-saving measure in 6 cases of paralysis of the respiratory muscles. Two patients with bulbar involvement were treated by the dehydration process; dextrose was given intravenously and magnesium sulfate intramuscularly, apparently with good results. The number of patients treated with convalescent serum was too small to be of any significance.

Buffum, Providence, R. I.

Varicella of the Cornea. R. Pickard, Brit. J. Ophth. **20**:15 (Jan.) 1936.

A boy 10 years of age was the last of four children in a family to contract varicella. Three weeks later one of his eyes became irritable. Two days after this the cornea showed a central gray opacity, well defined, circular, with a crenate edge, and, in diameter, equal to one quarter of the cornea. The pupil was sluggish. The biomicroscope showed a swelling of the cornea in the region of the opacity, bulging toward the anterior chamber. The section of the cornea was yellowish and mottled. On the posterior surface of the cornea was a flat brownish-yellow mass, having a free spongy surface. The corneal nerves were not thickened. The curve of the cornea was normal. There was full recovery of vision.

The aspects observed with the slit lamp suggest that the keratitis was caused by an organism having a limited growth, the course of which soon came to an end. The simplest explanation of the condition is that it was an eruption of varicella, occurring late because of the special structure of the cornea—a nonvascular dense tissue which offers special difficulties to the transit of the virus.

W. ZENTMAYER. [ARCH. OPHTH.]

DELAYED RASH IN MEASLES. ROBERT SELBY, Brit. M. J. **1**:262 (Feb. 8) 1936.

Selby reports two cases of measles, one in a girl aged 8 years on whom the rash appeared eleven days after the beginning of symptoms and the other in a boy 9 years old on whom the rash appeared nine days after the beginning of the condition.

ROYSTER, University, Va.

MEASLES AND CONVALESCENT SERUM. G. W. ELKINGTON, Brit. M. J. **1**:308 (Feb. 15) 1936.

Elkington describes his experience with an outbreak of measles in a school, with 100 per cent incidence. Convalescent serum was used. Some teachers felt that the epidemic was much ameliorated, and many children were prevented from having cough and toxemia.

ROYSTER, University, Va.

NASAL DIPHTHERIA CARRIERS. G. DE M. RUDOLF and W. R. ASHBY, J. Hyg. **36**: 129 (June) 1936.

A series of sixty-three institutional nasal carriers of morphologic Corynebacterium diphtheriae, virulent in some and avirulent in others, was studied. Treatment consisted in gargling with physiologic solution of sodium chloride and sniffing the solution up the nose three times a day. Nasal swabs were collected at irregular intervals until three yielding no diphtheria organisms were obtained. Since in twenty-two cases two such swabs in succession were followed by one carrying the organisms, two swabs without organisms are clearly insufficient in deciding that the carrier state has ceased. In nineteen cases in which the duration of the carrier state was known it was less than nine days. Of forty-three cases in which a duration of the carrier state was possible it was under nine days in thirty-one.

The swab test was computed to be reliable in identifying 65 per cent of carriers; five swabs per person are necessary to recognize 99 per cent of carriers.

Treatment with physiologic solution of sodium chloride appeared to reduce the number of swabs showing the organisms by two.

F. R. JANNEY, Wauwatosa, Wis.

THE INCIDENCE AND CLINICAL CORRELATION OF TYPES OF CORYNEBACTERIUM DIPHTHERIAE AT ROMFORD, ESSEX. R. W. TANNAHILL, J. Hyg. **36**:140 (June) 1936.

This is a study of 400 consecutive cases of diphtheria with particular reference to the correlation of the different types, gravis, intermedius and mitis, with the clinical findings.

The fatality rate was 9.5 per cent (38 deaths) for all cases, 13.8 per cent for the intermedius type, 9.5 per cent for the gravis type and 4.8 per cent for the mitis type.

Antitoxin (20,000 units for mild, 40,000 for moderate and from 80,000 to 120,000 units for severe diptheria) was given usually intermuscularly in one dose. This was given within one hour after admission and repeated in twelve hours if necessary. No patient was allowed to sit up before four weeks or to walk before six weeks.

Of the 38 deaths, 32 were due to toxicity, and 18 of these were of the hemorrhagic type (12 gravis and 6 intermedius). Laryngeal diphtheria (2.25 per cent) was found in all groups.

JANNEY, WAUWATOSA, WIS.

THE EARLY DIAGNOSIS OF INFANTILE PARALYSIS AND ITS TREATMENT. JAMES M. SMELLIE, Practitioner **136**:203 (Feb.) 1936.

Poliomyelitis has been defined as an acute infectious disease of the central nervous system, of both sporadic and epidemic occurrence. The infecting agent is a neurotropic virus that gains entrance to the nervous system along the fibers of the olfactory nerves from the nose or the nasopharynx. The infection is spread by healthy carriers, by persons with mild or abortive attacks and by those in the acute stage of the disease before paralysis has developed.

The three distinct clinical stages are as follows: (1) The first stage is characterized by a symptom complex which may simulate any acute infection; that is, there may be pyrexia, malaise, vague generalized pain, sweating, vomiting, mild diarrhea and coryza. Diagnosis during the first stage is almost impossible except during an epidemic. 2. The preparalytic period occupies from forty-eight to seventy-two hours. The general, or systemic, signs and symptoms include fever, sometimes continuous with the first stage, sometimes showing a secondary rise after having been normal for one or two days; tachycardia greater than the fever would indicate prostration, with anxious facies, nausea or even vomiting, and sweating. The neurologic findings are of the greatest importance. Headache is usually present. There may be pain in the neck, back or extremities. There may be unsteady voluntary movements or muscular twitchings. The finding of greatest importance is rigidity of the muscles of the lower cervical and upper dorsal region of the spine. Examination of the spinal fluid may supply valuable information. In poliomyelitis the pressure is usually increased, the cell count may vary widely from 50 to 600, or even higher, and the protein content of the fluid is increased. 3. The third stage begins with the onset of paralysis.

Differential diagnosis must include the various types of meningitis and conditions showing true paralysis or pseudoparalysis.

Under treatment the use of serum is carefully discussed. Serum may be derived from the following sources: (1) from patients in the convalescent stage of an acute attack, (2) from persons who have recovered from an attack even from ten to twenty years previously and (3) from normal adults with no history of ever having had the disease. The second-named serum, or human antiviral serum, is valuable only if laboratory tests show it to contain specific antiviral substance. The author stresses the point that the serum used must be given during the preparalytic stage to be of value. Repeated lumbar puncture may be an aid in the control of marked increase in fluid pressure.

For prophylactic use a serum prepared by immunizing horses with the virus of poliomyelitis will produce a passive immunity lasting for a few weeks and may be of distinct value during epidemics.

SAPPINGTON, San Francisco.

CERVICAL ADENITIS OF DIPHTHERITIC ORIGIN WITHOUT ANGINA OF MEMBRANES. ANDRÉASSIAN, Paris méd. **2**:90 (Aug. 1) 1936.

Andréassian describes two cases in which there was a sudden onset of fever with swelling of the glands of the neck. In both instances the throat showed only slight redness with a few small gray points on the tonsils. The cultures from the throat revealed diphtheria bacilli. Following the administration of antitoxin both patients made a prompt recovery.

LESLIE, Evanston, Ill.

THE RÔLE OF SERUM THERAPY IN PARALYSIS DUE TO DIPHTHERIA. ANDRÉASSIAN, Paris méd. **2**:92 (Aug. 1) 1936.

Andréassian objects to the statement of Ramon, Debré and Uhry that after the development of paralysis in diphtheria antitoxin is of no avail in bringing about improvement. He cites a case in which paralysis developed five weeks after a throat infection which was probably of diphtheritic origin and in which the condition responded very well to serum therapy instituted at that time.

LESLIE, Evanston, Ill.

A New Treatment of Diphtheritic Paralyses. P. Dodel and A. Foucher, Paris méd. **2**:110 (Aug. 15) 1936.

The authors have used water saturated with chloroform in the hope that the chloroform would replace the toxin bound in the lipoids of the nervous system. From 30 to 60 cc. was given by mouth each day. In some of the cases antitoxin was also given in doses of from 5 to 10 cc. Eleven cases are reported. Four patients treated with chloroform alone recovered from the paralyses within twenty-one days. Five treated with chloroform and antitoxin recovered in less than fifteen days. Two died from respiratory complications. The authors followed their patients for several months after the treatment and found no sign of hepatic injury. They admit that recovery from the paralyses might have taken place without treatment but at the same time think their method deserves consideration.

Leslie, Evanston, Ill.

Attempt at Prevention of Bronchopulmonary Infections in Measles. Chevalley, Duchon and Fourestier, Presse méd. **44**:766 (May 9) 1936.

In an attempt to curb the tremendous mortality from bronchopulmonary complications following measles, Chevalley, Duchon and Fourestier have employed a combination of preventive therapeutics. Feeling that, since in measles the respiratory tract is unusually vulnerable and that a relative state of immunity to the more virulent diseases of the throat and lower respiratory organs is insufficient, they administer to every child admitted to "Bastion 29" with measles 20 cc. of antidiphtheritic serum and 1 cc. of polyvalent vaccine. The vaccination is repeated daily for eight days. They have by this procedure reduced the mortality from 15.5 per cent in the untreated to 5.1 per cent in the treated group.

Bieker, St. Petersburg, Fla.

Reconstructive Treatment of Infantile Paralysis. Alberto Inclán, Cir. ortop. y traumatol. **2**:147 (July) 1934.

Inclán gives his experience during the past five years with the use of arthrodesis of the ankle by Campbell's bone-blocking method in the treatment of paralytic foot drop. When revising the joint in the last forty cases in which he operated for infantile paralysis he found that most of the interventions were practiced in order to reconstruct the paralyzed foot. Of thirty-three operations on paralytic feet, six were for correcting foot drop, and in these he employed the posterior osseus block after triple arthrodesis of the astragalocalcanean, astragalonavicular and calcaneocuboid articulations following the method of Campbell. He has discarded other procedures entirely. He describes the technic of the operation in detail and presents pictures and roentgenograms showing the results obtained.

Herron, Spokane, Wash.

Early Diagnosis and Treatment of Infantile Paralysis. Juan Bravo y Frias, Arch. españ. de pediat. **20**:5 (Jan.) 1936.

Bravo y Frias reports three cases of typical infantile paralysis, one in an infant of 13 months showing the typical picture of acute anterior poliomyelitis, the second in a child 6 years old showing the meningitic form, and the third in a child 4 years old showing the acute ascending bulbar type.

As a possible port of entry of the virus the nasopharynx is primarily concerned but is not the only one. The lungs and especially the gastro-intestinal tract are equally important as ports of entry. The author favors Toomey's theory of transmission of the virus and points out the frequent association of gastro-intestinal disorder with the early development of the disease. Inflammation of the mucous membrane of either the rhinopharynx or the gastro-intestinal tract or of both seems to be constantly present.

The author raises the question of neuropathy in the case of the antecedents as a possible predisposing factor. There also seems to be a seasonal factor.

Changes in the spinal fluid are the most reliable early signs of poliomyelitis. The author has seen no good effect from the use of convalescent serum. He has had the same experience with all other forms of therapy and expresses the belief that the only hope for future effective measures against the disease lies in prophylaxis and active immunization. He attaches great importance to postural and proper orthopedic treatment of the disease and complete immobilization in the early stages.

SCHLUTZ, Chicago.

MENINGOCOCCIC MENINGITIS PRODUCED BY A MENINGOCOCCUS OF ATYPICAL FORM. PEDRO QUERO PRETEL, Arch. españ. de pediat. **20**:146 (March) 1936.

Quero Pretel reports a case of meningococcic meningitis of this type in an infant aged 9 months. The blood of such patients does not agglutinate with the ordinary serums of the laboratory and is resistant to all forms of serum treatment. The prognosis is always grave but particularly so in the very young infant. In the treatment of meningococcic meningitis, the author gives the serum by the intraspinal, cisternal and intravenous routes.

SCHLUTZ, Chicago.

ENCEPHALITIS FOLLOWING PERTUSSIS. CARLOS GIANELLI, Arch. de pediat. d. Uruguay **7**:14 (Jan.) 1936.

Gianelli reports the occurrence of encephalitis in two infants in whom it developed in the fifth and sixth week of the attack. Convulsions and various paralytic manifestations were the most prominent symptoms. The spinal fluid was clear but had a markedly increased dextrose content. Both patients acquired bronchopneumonia, which terminated fatally. There were no autopsies.

SCHLUTZ, Chicago.

ALASTRIM. JOSÉ M. DA ROCHA, J. de pediat., Rio de Janeiro **3**:92 (Feb.) 1936.

Alastrim (Kaffir milk pox) has a mortality of from 0.5 to 2 per cent. It was first described in Brazil by Ribas in 1910. The incubation period is from sixteen to twenty-one days. The eruption is a cross between chickenpox and smallpox. It has been shown to be a distinct disease entity by the inoculation of animals by Blaxall. The treatment is the same as that for smallpox. Isolation is the only prophylaxis.

SANFORD, Chicago.

IS THERE AN INTESTINAL DIPHTHERIA CAUSED BY LOEFFLER'S BACILLI? JOSÉ M. DA ROCHA, J. de pediat., Rio de Janeiro **3**:357 (Aug.) 1936.

Da Rocha does not believe that true intestinal diphtheria exists, as the abundance of colon bacilli would serve to kill the diphtheria organism. Experimental work serves to bear out this point. He does not believe that reported cases have been proved to be what they are claimed to be (this statement does not include Barboza's case reported in the same issue).

SANFORD, Chicago.

THE TREATMENT OF POLIOMYELITIS WITH CONVALESCENT SERUM IN GERMANY. H. SCHLOSSBERGER and T. LINK, Paidoterapia **14**:1045 (March) 1936.

The use of convalescent serum in the treatment of poliomyelitis as described in both the foreign and the American literature is reviewed, and it is found that in the American literature much value does not seem to be given to its use, whereas more credit is given in the European literature. Since this illness produces great mortality and paralysis it was decided in Germany to improve the therapy, and since 1932 accurate statistics have been kept. It has been shown that the use of the serum does more good early in the disease, especially in the preparalytic stage. Large doses of serum are given. There is a method for organized collection

of convalescent serum. All physicians are required to inform the authorities as to persons who have had poliomyelitis since 1929 and who could be considered as suppliers of blood. Every six months the new cases are reported. The results of this campaign are not satisfactory, however, as only 35 per cent of the summoned ones have supplied blood; the majority of these reside in orthopedic clinics and institutions. However, as this organization has been formed only recently a better result is to be hoped for, along with the collaboration of those who have benefited by this therapy.

HERRON, Spokane, Wash.

EPIDEMIC PAROTITIS AND MENINGO-ENCEPHALITIS. GUILLERMO ARCE, Pediatría españ. **25**:55 (March) 1936.

Arce gives a general discussion of this condition without a report of cases. He subscribes to the theory of Montgomery that epidemic parotitis is produced by a cytoneurotropic virus which has a predilection in its localization for the nervous system, the salivary glands, the pancreas and the gonads. It may, depending on certain conditions, affect several or all of these parts, or it may affect exclusively one part, such as the meninges, and can then produce meningo-encephalitis of the type described by Weissenbach. This form of meningo-encephalitis is rarely fatal, and the prognosis is good. Convalescent serum has given good results in the treatment.

SCHLUTZ, Chicago.

ALLERGY IN DIPHTHERIA. OTTOKAR CHIARI and JOSEF SIEGL, Arch. f. Kinderh. **105**:65, 1935.

Investigation has demonstrated that in the great majority of cases of diphtheria a specific allergy of varying degree to Bacillus diphtheriae appears in the latter half of the first week of the disease. This usually persists only from two to three weeks and then disappears. In patients who are treated late it persists somewhat longer. In the judgment of the authors, the observation of the development and disappearance of a specific sensitivity as a result of an attack of diphtheria gives evidence that the defense mechanism against diphtheria does not consist of antitoxin alone but that other biologic processes, for example, such a specific sensitization as is here described, must be assumed.

CRANE, Chicago.

MENINGOCOCCIC SEPSIS. HANS WEITKAMP, Kinderärztl. Praxis **7**:73 (Feb.); 117 (March) 1936.

Weitkamp reviews the literature on meningococcic sepsis and gives observations on six cases of his own. He arrives at the following conclusions: Meningococcic meningitis is always only a symptom of meningococcic sepsis. Cases have been reported in which the infection of the meninges started as late as two months after the onset of the bacteremia, as well as cases in which meningococci were found in the blood stream for four months without the patient's ever having suffered from meningitis. The most outstanding symptom of meningococcic sepsis is a hemorrhagic rash; such a rash may also be produced, however, by other bacteremias than those due to meningococci, such as staphylococcic bacteremias. The petechiae have necrotic, purplish centers and represent bacterial emboli. They may also be found on the mucous membranes, so that in severe, acute sepsis it may be difficult, in making the diagnosis, to differentiate the condition from purpura fulminans. The author expresses the belief that in cases in which there is a hemorrhagic rash the prognosis is worse than in those without the rash. Whenever hemorrhage occurs in the adrenal glands (where it may take place as well as in the skin), a fully developed picture of Waterhouse-Friedrichsen's disease (or symptom complex) may be produced. The author suspects that this disease, which affects chiefly infants under 2 years of age, may be merely a special form of meningococcic sepsis in most of the cases reported. He suggests that blood cultures be taken in every instance, as this assumption finds support in Bamatter's

studies (*Jahrb. f. Kinderh.* **142**:129, 1934). Other suggestive findings in meningococcic sepsis are iridochoroiditis, uveitis and nephritis. The value of serum in meningococcic sepsis seems doubtful. The best results are reported from blood transfusions. The use of adrenal preparations in Watterhouse-Friedrichsen's disease is indicated, although their value remains uncertain.

HEYMANN, Cleveland.

DIPHTHERITIC LARYNGEAL STENOSIS. C. A. BAU, Klin. Wchnschr. **14**:1781 (Dec. 14) 1935.

Bau reports his experiences with diphtheritic laryngeal stenosis at the Clinic for Infectious Diseases of Düsseldorf. His observations cover the period from 1926 to 1934. In recent years conservative treatment has been supplemented with intubation or tracheotomy or both in a large percentage of the cases. The treatment in outline was as follows: The child is isolated in a quiet room and is constantly under the care of a nurse. Immediately on entrance to the clinic he is given 10,000 units of antitoxin intravenously. Then 6,000 units is given intramuscularly at intervals of from three to six hours until the membranes are partially cast off. Cardiac stimulants and drugs to relieve the dyspnea may be given.

The membranes may be sucked off with a pump. Children with mild diphtheritic laryngeal stenosis are not intubated or tracheotomized. In cases of severe involvement these procedures are postponed until the serum has had opportunity to take effect. In recent years intubation has been more frequently used at the Düsseldorf Children's Clinic, although formerly it had been discarded. When intubation gives no relief, it is followed at once by tracheotomy. Extubation should be delayed for about seventy-two hours because successive intubation may produce such edema of the larynx that tracheotomy may be unavoidable.

ABT, Chicago.

PATHOLOGIC EXAMINATION IN A CASE OF POSTVACCINAL ENCEPHALITIS IN WHICH RECOVERY OCCURRED. BERND HERKENRATH, Ztschr. f. d. ges. Neurol. u. Psychiat. **152**:293 (March) 1935.

Herkenrath makes the only report in the literature of a pathologic study of postvaccinal encephalitis in which recovery took place. A girl, aged 3 years, was vaccinated after a previous unsuccessful vaccination about seven months before. There was a history of a convulsion at the age of 2 years and of chickenpox about one month before examination. Six days after vaccination the child became febrile, vomited and had a convulsion, which was more marked on the left side. The next morning she had hemiplegia on the left side. She was drowsy, had spastic hemiplegia on the left side and reacted poorly to pinpricks on that side of the body. There were no signs of involvement of the meninges; there was a Babinski sign on the left; there were no differences in the tendon reflexes; the abdominal reflexes were diminished on the left. Lumbar puncture yielded fluid under a pressure of 160 mm. of water, containing 10 cells per cubic millimeter and 72 mg. of sugar per hundred cubic centimeters. The Pandy and Nonne-Apelt tests gave negative results. On the third day she had a morbilliform exanthem on the palms and soles. A number of focal convulsive seizures occurred on the left side during the course of the disease, and on one occasion a seizure occurred in the right upper limb. Her condition improved progressively. Neurologic examination twenty-five days after admission to the hospital showed no positive neurologic signs and no changes in the mental status. She was discharged as recovered fifty-five days after admission. Three months later she was reexamined. Relatives reported that she was somewhat irritable. Neurologic and mental examinations gave negative results except for inability to speak as clearly as before the encephalitis.

Sixteen months after discharge the child was readmitted to the hospital with Vincent's angina. At that time neuropsychiatric examination gave negative results. The irritability and the speech defect were no longer present. About one and one-half years after discharge she died of an intercurrent infection.

Examination of the internal organs revealed no significant changes. Grossly the brain was normal. Careful microscopic examination, utilizing all modern technics, showed only some fat-laden scavenger cells in the perivascular spaces of the cerebellum, pons, medulla and spinal cord. Most of these cells were small and round. These gitter cells were especially frequent in the venous perivascular sheaths. There was no evidence of perivascular, subependymal or cortical gliosis. There were no changes in the myelin sheaths. No alterations were present in the ganglion cells except in the temporal lobes and in the right lateral nucleus of the thalamus, where there was a relatively marked atrophy of cells with diffuse increase of the smaller glia cells.

The only pathologic evidence, therefore, of the previous condition of the brain was the presence of perivascular gitter cells. There were no other perceptible residual signs of the severe, infectious disease of the nervous system. The neural parenchyma was intact. Herkenrath refuses to consider the local tissue changes in the temporal lobes and in the lateral nucleus of the thalamus as sequelae of the encephalitic process. In addition to the unusual localization of these tissue changes for postvaccinal encephalitis, he notes the relatively frequent finding of such changes in the brains of children as a result of focal functional vascular changes. The conclusion is therefore warranted that there may be not only complete clinical recovery but also anatomic restitutio ad integrum.

SAVITSKY, New York. [ARCH. NEUROL. & PSYCHIAT.]

PERMANENT CARDIAC DISORDER FOLLOWING DIPHTHERIA. P. KISS, Orvosi hetil. **79**:972 (Sept. 7) 1935.

A boy 8 years of age was admitted to the clinic in Budapest with vomiting and gastric pain. Three weeks before his admission he had had pain in his throat. The parents saw a white membrane then, but no physician had been called. The examination in the clinic showed paralysis of the soft palate. The throat was clear, but diphtheria bacilli were present. There was severe myocarditis. Later the right arm and leg were paralyzed by emboli. He lay three months in the clinic, and the disorders continued after he was taken home. He was examined five years later. The spastic hemiplegia of the right side was still present. There were no clinical alterations in the heart, but the electrocardiographic examination showed that the disorder of intraventricular leading and some disorder of the myocardium had become permanent.

GÖTTCHE, Budapest, Hungary.

ELECTROCARDIOGRAMS OF CHILDREN WITH TYPHOID. P. KISS and B. WOLLEK, Orvosi hetil. **79**:1339 (Dec. 21) 1935.

A disorder of the vasomotor nerves does not produce any alteration in the electrocardiogram. The differentiation of arrhythmias during typhoid in childhood is possible only by electrocardiographic examination. These arrhythmias are mostly respiration arrhythmias; other arrhythmias are caused by myocarditis. In these cases the QRS complex shows the greatest alteration. The myocardial alterations may occur without any clinical signs: The pulse is normal, auscultation of the heart does not show any disorder and the general condition of the child alone calls attention to the cardiac disorder. The progress of the recovery also can be followed by electrocardiographic examinations.

GÖTTCHE, Budapest, Hungary.

THE STUDY OF WHOOPING COUGH IN INFANTS. GEORGE BRDLÍK, GEORGE POKORNY, IVAN HEČKO and MARGITA STOLZ-SUTORIS, Časop. lék. česk. **73**:281 (March 16) 1934.

The clinical findings are discussed by Professor Brdlík. During a recent epidemic only 71.43 per cent of infants in intimate contact with patients in whom the disease was active contracted pertussis. This was a small group under 10 months of age, breast fed and artificially fed, made up of syphilitic children, well children of syphilitic mothers and boarder babies; so no generalization could be made as to causes. Against the idea that pertussis is not contagious after the primary stages Brdlík cites several cases in which virulent Bordet-Gengou organisms were cultured seventy-seven and ninety-four days after the onset. Spasmodic cough began in ten children on the fifth day and in four on the first day. The incubation period varied from five to twenty-one days. The characteristic findings were edema of the lids, prominence of the eyeballs and, less frequently, subconjunctival hemorrhage. Four infants expectorated, and all but four vomited. Emphysema remained as long as eighty days in some cases. Increase in the hilar silhouette was noted in some instances. Elevation of temperature is usually associated with some complication, as bronchitis or bronchopneumonia. Pertussis lowers the resistance to infection, so that all the infants came down with grip in the current epidemic. All of the infants had negative Pirquet reactions. The therapy was directed at symptoms and included sedation in spite of the fact that some authors feel that the complications are inversely proportional to the severity of the cough.

STULIK, Chicago.

THE HEMATOLOGY OF PERTUSSIS. GEORGE POKORNY, Časop lék. česk. **73**:288 (March 16) 1934.

The increased lipoid content of Bordet-Gengou bacilli is regarded as a factor in the leukocytosis and relative lymphocytosis. No prodromal leukopenia was noted even in some patients tested several days before the onset of symptoms. Normal leukocyte counts were found at the onset, with gradually increasing counts up to the culmination of the disease, then a gradual return to par. The highest lymphocytosis was found about the seventh day, i. e., an increase of about 70 per cent, and the highest white blood cell count was 81,250, which was found for a patient with relatively mild pertussis. Some authors feel that the disease is infectious as long as the leukocytosis persists. In some instances the count was increased 50 to 70 per cent at the onset of a paroxysm and receded in about fifteen minutes. The counts were made several hours after ingestion of food, to obviate the effect of food on the count.

STULIK, Chicago.

THE CAPILLAROSCOPIC FINDINGS IN PERTUSSIS. IVAN HEČKO, Časop. lék. česk. **73**:293 (March 16) 1934.

R. Hess thinks that the postparoxysmal increase in the white blood cells is due to the stripping of the spleen and thoracic duct during the paroxysm. Hečko feels that the increase is due to the temporary stagnation in the peripheral circulation and the accumulation of white cells in the dilated fine veins from which the blood is obtained in the puncture. This accumulation persists until normal circulation is reestablished between spells.

STULIK, Chicago.

THE BACTERIOLOGIC, SEROLOGIC AND EPIDEMIOLOGICAL FINDINGS IN PERTUSSIS. MARGITA STOLZ-SUTORIS, Časop. lék. česk. **73**:295 (March 16) 1934.

A résumé of the discovery, microscopy, bacteriology and cultural attributes of the Bordet-Gengou bacillus is given. The epidemic described apparently began in an infant transferred from the new-born infant service after one month. Most likely the infection was brought in by a carrier, as cultures taken from the throats of the entire staff, both medical and nursing, were negative. Cultures were made according to the method of Legroux, and the organism was identified by inoculation in guinea-pigs. Most cultures were negative after the thirtieth or fortieth

day of the disease. Agglutination in dilutions of from 1:1,000 to 1:2,000, and complement deviation were specific and were positive usually in from ten to fourteen days and, in several instances, in from five to seven days, after the onset. In four cases no development of antibodies took place even after injection of polyvalent vaccine, and this failure was considered to represent a congenital inability to form antibodies.

WALLGREN, Gothenburg, Sweden.

SMALLPOX VACCINATION IN CHILDHOOD IN VIEW OF THE EFFECT OF VACCINATION IN THE SWEDISH ARMY. CURT GYLLENSVÄRD, Tidskr. i militär hälsovård **60**:93, 1935.

Formerly one had the opinion that from 50 to 90 per cent of all soldiers vaccinated in childhood had lost their immunity. Gyllensvärd has now studied the reports of about 750,000 vaccinations made during the period from 1908 to 1933 and has found that the reactions, with only few exceptions, were of the type that von Pirquet described as a hastened, allergic (i. e., immune) response. From this it ensues that a relative immunity is still present twenty years after the first vaccination. Persons on whom the first vaccination was made at the age of 20 show much more severe symptoms than revaccinated persons of the same age who had their first vaccination at the age of 2. It is suggested that two scars be made and that the inoculated area be inspected four days after vaccination in order to avoid overlooking the allergic reaction. In a series of 9,000 vaccinations made according to this rule it was found that 96 per cent resulted positively as compared with only 80 per cent when inspection was done eight days after inoculation.

WALLGREN, Gothenburg, Sweden.

SERUM TREATMENT OF SCARLET FEVER. OLE BANG and OLE FREDERIKSEN, Ugesk. f. læger **98**:503 (June 4) 1936.

The authors cite the literature and give their experience gained at the Blegdems Hospital.

Scarlet fever convalescents' serum is preferred. Both scarlatinal antitoxin and scarlatinal convalescents' serum possess marked antitoxic properties, but there seems to be no indication of any definite effect in regard to complications.

ELGHAMMER, Chicago.

THE DICK REACTION AND IMMUNITY TO SCARLET FEVER. OSWALD BRINCH, Ugesk. f. læger **98**:689 (July 23) 1936.

Among twelve children exposed to scarlet fever, the Dick test was found to be negative in seven and positive in five. Two children in whom the test was negative contracted scarlet fever. Among the children in whom the test was positive each of whom received 10 cc. of scarlatinal convalescents' serum, one contracted the disease. Brinch points out that the Dick test performed with monovalent toxin is not a reliable indication of immunity to scarlet fever.

ELGHAMMER, Chicago.

## Acute Infectious Diseases

AMOEBIASIS AND BACILLARY DYSENTERY IN THE LOS ANGELES COUNTY HOSPITAL, 1929-1935. J. F. KESSEL, L. BLAKELY and K. CAVELL, Am. J. Trop. Med. **16**: 417 (July) 1936.

The authors made a study of stools or of material obtained in the course of proctoscopic or sigmoidoscopic examinations from all patients with dysentery or diarrhea admitted to the inpatient or outpatient departments of the Los Angeles County Hospital over a period of six years (1929-1935). They found that dysentery in southern California was caused primarily by three types of micro-organisms: Shigella paradysenteriae, Salmonella Morgani and other species of Salmonella, and Endamoeba histolytica. Acute bacillary dysentery was encountered much more frequently than acute amebic dysentery, but chronic amebiasis was more common than chronic bacillary dysentery.

BURPEE, Augusta, Ga.

TRIATOMA DIMIDIATA LATR. NATURALLY INFECTED WITH TRYPANOSOMA CRUZI A CAUSE OF CHAGAS' DISEASE IN PANAMA. L. E. ROSEBLOOM, Am. J. Trop. Med. **16:** 481 (July) 1936.

Rosebloom examined a number of Triatoma dimidiata Latr. taken from the homes of natives in Panama and found them infected with Trypanosoma Cruzi. These bugs come out at night to feed on the inhabitants and particularly on children. Thus a fourth vector of Chagas' disease is found in Panama.

BURPEE, Augusta, Ga.

SOME OBSERVATIONS ON THE NATURE OF THE THERMOPRECIPITATION REACTION IN TRYPANOSOMA EQUIPERDUM INFECTION. H. A. POINDEXTER, Am. J. Trop. Med. **16:** 485 (July) 1936.

Poindexter discusses briefly some of the difficulties encountered in making a diagnosis of trypanosomiasis in man or animal and describes numerous experiments performed in an attempt to simplify the diagnosis.

Former experimental work along this line raised the following questions: What is the nature of the thermostable precipitinogenic substance and what is the nature of the reaction? What organs of the body will yield tissue extracts giving the better reaction, and why? From what laboratory animal may the most active extracts be produced, and what animal shows immune serum of the highest titer?

Extracts were prepared from various tissues and organs of animals that had died from infection with T. equiperdum, and their chemical nature and thermoprecipitinogenic action were studied.

From these experiments Poindexter concludes that the thermostable substance extracted from the tissues of animals infected with T. equiperdum appears to be a "co-mingled" protein, though a large portion of it may be a carbohydrate. The extracts of the organs that are more active in hematopoiesis and hemoclasis contain the greatest amounts of the thermoprecipitinogenic substance. The titer of the serum from infected rabbits was higher than that of serum from other infected laboratory animals tested.

BURPEE, Augusta, Ga.

STUDIES ON THE MECHANISM OF IMMUNITY IN TYPHUS FEVER: III. DEMONSTRATION OF OPSONINS FOR RICKETTSIA PROWAZEKI IN TYPHUS-IMMUNE SERUM. M. RUIZ CASTANEDA, J. Immunol. **31**:227 (Sept.) 1936.

The author has demonstrated opsonins for Rickettsia Prowazeki (Mexican type) in the serums of guinea-pigs recovered from or infected with either Mexican or European typhus. Opsonins were demonstrated in the serums of human beings from two to six years after recovery from Brill's disease. These demonstrations were made by preparing a mixture of serum, fresh defibrinated blood of a normal guinea-pig, and a suspension of rickettsias. The suspension of rickettsias was obtained from peritoneal washings of roentgen-irradiated rats infected with Mexican typhus. Such mixtures were incubated for one hour in a rotating machine; smears were prepared, stained and examined for phagocytosed rickettsias.

Antiproteus X 19 serum failed to opsonize the rickettsias of Mexican typhus.

FOTHERGILL, Boston.

INFLUENCE OF THE TONSILS ON RHEUMATIC INFECTION IN CHILDREN. ALBERT D. KAISER, J. Lab. & Clin. Med. **21**:609 (March) 1936.

Tonsillectomized children have a 35 per cent better chance of escaping rheumatic fever than do those with tonsils. The incidence of muscular rheumatism and chorea is not influenced by tonsillectomy. The incidence of recurrence was not found to be influenced by tonsillectomy. The mortality among rheumatic children who had been tonsillectomized was about half that for children who had not been tonsillectomized. Kaiser concludes that practically every child who shows any rheumatic manifestation should have his tonsils removed.

MCMURRAY, Galveston, Texas.

DISCUSSION OF PAPER BY DR. HUGH MCCULLOCH, "INSTITUTIONAL PROVISIONS FOR THE CARE OF THE RHEUMATIC CHILD." W. D. STROUD, J. Lab. & Clin. Med. **21**:618 (March) 1936.

Stroud recommends tonsillectomy for all rheumatic children. He also expresses the belief that institutional care is of definite benefit to all children with rheumatic heart disease.

MCMURRAY, Galveston, Texas.

BACTERIOLOGIC STUDIES OF THE BLOOD OF NORMAL PERSONS AND OF PATIENTS WITH RHEUMATIC FEVER. ESTHER MEYER and VIRGINIA RYAN, J. Lab. & Clin. Med. **22**:113 (Nov.) 1936.

Bacteriologic studies were made of the blood of rheumatic children, normal children and normal adults. Each specimen of blood was cultured on both Kendall's fluid medium and dextrose-calcium carbonate veal infusion broth. The technic followed in this study is given in detail. The authors were unable to find any difference in the bacterial flora of the blood of children with rheumatic fever, normal children and normal adults.

MCMURRAY, Galveston, Texas.

THE DIAGNOSIS OF BRUCELLA INFECTION IN ANIMALS AND MAN BY RAPID MICROSCOPIC AGGLUTINATION. I. F. HUDDLESON, Michigan Agric. Exper. Stat., Tech. Bull. 123, January 1932.

Two methods are described for preparing rapid antigen for detecting specific agglutinins in the blood serum of animals and man corresponding to infections with Brucella melitensis, Brucella abortus and Brucella suis. The technic of the rapid test for agglutinin and its interpretation are also presented.

VINTON, New York.

A CASE OF POSTGRIPPAL MYOCLONIA IN AN INFANT. HENRIETTE V. CONSTANTINESCU, Bull. Soc. de pédiat. de Iasi **6**:44 (April-June) 1935.

The patient, an infant of 9 months, was brought to the clinic because of repeated twitchings. These were more apparent in the upper extremities but occurred also in the legs, although here the myoclonia was masked by voluntary movements. The cerebrospinal fluid was normal, and the child showed no fever or other signs of illness. The history disclosed that ten days previously the child had suffered from a moderately severe infection of the respiratory tract. In the discussion two other cases of myoclonia following grippal infections are reported.

LESLIE, Evanston, Ill.

VACCINATION AGAINST TETANUS. CHILDREN SHOULD BE VACCINATED AGAINST TETANUS AND SHOULD HAVE THE BENEFIT OF MIXED VACCINES. A. BOHN, Rev. méd.-sociale de l'enf. **4**:161 (May-June) 1936.

One should vaccinate children against tetanus. Recently there have been reported cases of tetanus in which the virus got into the body in ways other than through the skin, for example, through an infected ear or the cavity of an extracted tooth, or even without any recognized entrance. Besides, there are frequent reactions from passive immunization, sometimes serious, and immunization lasts only from twenty to twenty-five days.

Antitetanic toxoid is simple to use, produces no reaction, especially in the child, and gives a certain immunity. The only drawback is that it takes a period of time to establish the immunity, whereas serum gives immediate immunity.

Antitetanic vaccination is attained through three subcutaneous injections, at three week intervals, of Ramon's toxoid from the Pasteur Institute.

It is advised that all children be vaccinated at from 18 to 20 months or later, tetanus and diphtheria toxoid being combined in the first two injections. These toxoids are obtainable from the Pasteur Institute already mixed, separate or

combined with typhoid-paratyphoid vaccine as desired. Every four to five years another "shot" of mixed vaccine should be given in order to renew the immunity. There is no test for immunity to tetanus analogous to the Schick test.

Dr. Bohn has given antitetanic vaccine as a routine for several years in all cases in which the parents consented.

BROWNE, Detroit.

THE USE OF AMINOPYRINE IN INFANTILE TYPHOID. EMILIO COMENDADOR, Paidoterapia **13**:897 (Jan.) 1935.

Comendador reports two cases of typhoid in infants in which aminopyrine was used and excellent results obtained. He states that he does not intend to draw conclusions from only two cases but would like further study to see whether the method proves of value.

HERRON, Spokane, Wash.

GENITAL GONORRHEA IN INFANTS. F. GÓMEZ, E. SALGADA PALSCIOS and E. GONZÁLEZ, Rev. mex. de puericultura **5**:889 (Nov.) 1934.

The authors prefer "genital gonorrhea" to other terms. The disease is most often due to contamination from clothes. Clothes sterilized in a 10 per cent concentration of saponated solution of cresol gave after fifteen minutes 60 per cent positive cultures, after one hour 40 per cent, and after two hours 40 per cent. But after five hours in a 50 per cent concentration of the solution clothes gave 100 per cent negative cultures. The authors sterilize such clothes by immersion for twenty minutes in a 2 per cent concentration of the solution maintained at 110 F.; this results in 100 per cent negative cultures. They describe the numerous forms of treatment and prefer anhydrous wool fat ointment containing 2.5 per cent silver nitrate, which is instilled in the vagina under pressure. They have a series of twenty-four cases and report six in detail, with illustrations that portray the involvement of the cervix in these six cases. The bibliography is taken mostly from the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

HERRON, Spokane.

## Chronic Infectious Diseases

INCIDENCE OF TUBERCULOSIS IN CHILDREN ENTERING PRIMARY SCHOOLS IN VANCOUVER, BRITISH COLUMBIA. A. R. J. BOYD, Am. Rev. Tuberc. **34**:67 (July) 1936.

In an effort to trace tuberculous infection among school children to the sources, the primary class was selected as being most likely to have contacts with the disease at home. These children were tested with tuberculin, those showing positive reactions were roentgenographed, and the homes of those with positive findings were visited in a search for the sources of infection.

Positive reactions to tuberculin were found in 19.49 per cent of 1,001 children 6 years old. The majority of the reactors were not sensitive to 0.1 cc. of a 1:1,000 dilution of old tuberculin. They showed sensitivity only when a 1:100 dilution was used. A much higher percentage of positive reactions was obtained among small groups of oriental children. Tuberculous lesions were demonstrated in the x-ray plates of 13.22 per cent of the positive reactors. In the quest for contacts, 72 families were investigated, 51 completely. Sources of infection were found in 21 families.

EUGENE SMITH, Ogden, Utah.

CONTACT AS A FACTOR IN THE TRANSMISSION OF TUBERCULOSIS. CHARLES SCHUMAN, Am. Rev. Tuberc. **34**:85 (July) 1936.

A study of 3,057 persons attending a clinic for tuberculosis was made to determine the relative importance of different types of exposure in the dissemination of the disease. Among 1,802 adults were 730 with definite tuberculosis, and among 1,255 children, 47. Schuman states that a study of these tuberculous persons gave conclusive evidence that sputum containing tubercle bacilli is the greatest single factor in the spread of pulmonary tuberculosis, and that this is particularly true

of tuberculous infection in children. Persons in contact with tuberculous patients and exposed to such sputum show increased sensitivity to tuberculin. It follows that the most effective means of limiting the spread of the disease is the control of the patients whose sputum contains the bacilli.

EUGENE SMITH, Ogden, Utah.

JUVENILE PARETIC NEUROSYPHILIS STUDIES: III. DEVELOPMENTAL HISTORY. WILLIAM C. MENNINGER, J. Nerv. & Ment. Dis. **81**:389 (May) 1935.

This paper is a continuation of Menninger's studies on juvenile dementia paralytica and is concerned with the mental and physical development of the patient and with psychic trauma, physical trauma and the frequency of convulsions. Forty per cent of 426 patients with juvenile dementia paralytica were fundamentally retarded in mental development. In 60 per cent the mental development was normal until the onset of the disease. A brief report is made of 67 cases of hypophrenia, congenital syphilis being the etiologic factor in 29.8 per cent. Menninger declares that hypophrenia in cases of juvenile dementia paralytica is in no way different from other forms of mental deficiency but concludes that it is incorrect to assume that juvenile dementia paralytica develops in feebleminded persons. Psychic trauma was reported as a precipitating factor in 18 of 653 cases. Normal physical development occurred in 50 per cent of 349 cases. In 35 per cent there was retarded development which results in a kind of infantilism, though rarely of the Lorain type. It is primarily an arrest of growth with a stunted development and consequently a poorly proportioned body. Physical trauma is recorded in 35 of the 349 cases and is regarded merely as a precipitating factor. Convulsions were recorded in the history in 111, or 31.8 per cent, of cases in which adequate data were available. Convulsive seizures occurring prior to other symptoms and signs of juvenile dementia paralytica may be typical of and indistinguishable from the convulsions occurring in cases of idiopathic epilepsy.

HART, Greenwich, Conn. [ARCH. NEUROL. & PSYCHIAT.]

THE PRESENT STATUS OF ROENTGEN INTERPRETATION OF PULMONARY TUBERCULOSIS IN CHILDREN. KENNETH D. A. ALLEN, Northwest Med. **34**:238 (July) 1935.

Allen stresses the importance of knowing the phase of respiration at which the roentgenogram is taken. The distance between the inner end of the clavicle and the highest point of the diaphragmatic arch bears a constant relationship to the width of the chest—2:3 in inspiration and 1:2 in expiration.

Exposures should be less than one twentieth of a second, and the target-plate distance should not be less than 4 feet (120 cm.). Exposures should be made in various oblique and lateral positions. Serial films should be made at short intervals to detect evanescent infiltrations and evanescent changes in existing lesions.

The remainder of the article is concerned with the interpretation of a number of roentgenograms illustrating the childhood type of tuberculosis. For these the reader is referred to the original article.

SCOTT, Philadelphia.

FOLLOW-UP STUDY OF TUBERCULOUS CHILDREN DISCHARGED FROM SEA VIEW HOSPITAL. BÉLA SCHICK, HAROLD ROSENBERG and CAMILLE KERESZTURI, Quart. Bull., Sea View Hosp. **1**:314 (April) 1936.

The group studied comprised 629 patients, or about one third of all children discharged from the hospital during the past ten years. They were selected at random, but roentgenograms of their chests were available for study and classification. The death rate for all children in the pediatric service of the hospital during this period was 10.4 per cent. The death rate of the 629 children with pulmonary tuberculosis during hospitalization and after discharge was 14.4 per

cent; 93.3 per cent of the deaths in this group occurred within the first two years after admission. There were no deaths from tuberculosis among 135 children whose roentgenograms showed no thoracic disease but whose tuberculin tests were positive when they were admitted to the hospital. Only 0.7 per cent of the 142 children with tracheobronchial tuberculosis died. The children with pleurisy with effusion, nondestructive pulmonary infiltrations and fresh primary complexes showed, respectively, 5.7, 7.8 and 11.9 per cent deaths from tuberculosis. The highest mortality from tuberculosis occurred in the children with disseminated and miliary tuberculosis and destructive pulmonary infiltrations, i. e., 68.4 per cent and 68.7 per cent, respectively.

EUGENE SMITH, Ogden, Utah.

TUBERCULOSIS OF THE CHOROID ASSOCIATED WITH GENERALIZED MILIARY TUBERCULOSIS. F. TOOKE, Brit. J. Ophth. **20**:23 (Jan.) 1936.

A male infant of 13 months suddenly became irritable and was seized with vomiting, fever and a series of convulsions. During one of the attacks the eye and head were turned to the right. Chvostek's sign was present. The anterior cervical glands were enlarged; the posterior ones were small and shotty. The spinal fluid was clear and contained only 2 cells per cubic millimeter. The intradermal test with tuberculin gave positive results. A roentgenogram of the chest showed the lungs peppered or mottled with innumerable tubercles. In the right fundus there were at least seven tubercles, and in the left five, probably more. They were situated between the disk and the macular area and occurred as a cluster or group. They bore no relation to the retinal vessels, which were uninvolved. The surfaces of the disks were a good color and their margins sharply defined. Death occurred twenty-three days after the patient's admission to the hospital.

The postmortem observations and the pathologic anatomy of the eyeballs are given in detail. There was complete absence of any meningeal pathologic process in either the optic nerve or the subdural or vaginal spaces. The author's summary follows:

"Tubercles of the choroid are established as a haematogenous infection in a condition of a generalized miliary tuberculosis.

"Tuberculous meningitis results from contact with necrotic foci from adjacent tissues earlier involved through the blood stream.

"Tuberculous meningitis is a late rather than an early manifestation of the course of the disease.

"Tubercles of the choroid in certain cases are coincident rather than complicating manifestations of tuberculous meningitis.

"Tubercles of the choroid may exist not because of, but in spite of, tuberculous meningitis."

The article is illustrated. ZENTMAYER, Philadelphia. [ARCH. OPHTH.]

COURSE, COMPLICATIONS AND PROGNOSIS OF OPEN PULMONARY TUBERCULOSIS IN CHILDREN. E. COCHRANE, Tubercle **16**:529 (Sept.) 1935.

That open pulmonary tuberculosis is not invariably and rapidly fatal in young children appears from Cochrane's study of 710 cases (240 boys and 470 girls). All these children had tubercle bacilli in the sputum except 27, whose feces nevertheless gave a positive reaction. The disease ran a rapid and fatal course, from one to nine months, in 107 girls and 31 boys. On the other hand, it pursued a longer course in 164 girls and 94 boys, who lived from two to ten years after admission. Another group of 81 girls and 50 boys were discharged alive and completely or partially cured.

The three great sign posts of progress in children are temperature, pulse rate and weight, and weight is the most accurate index of the true state of affairs. As a rule, it may be maintained that the child who is overcoming infection will manifest this fact by growth. The pulse rate is valuable as an indicator of

toxemia, but it must be recorded only after a period of rest. The temperature likewise is subject to such frequent variations in childhood from a host of non-pulmonary conditions that these must be carefully excluded in drawing conclusions as to its significance.

Among the complications encountered in this group, hemoptysis is noteworthy, since it occurred in 100 girls and 47 boys. At any stage of the disease its appearance is of unfavorable import. Laryngitis developed rather frequently in the more chronic cases. Spontaneous pneumothorax occurred 14 times in girls, resulting in 13 deaths, and in 10 cases among boys, 5 of whom died almost immediately. Fifteen per cent of the 117 deaths in the hospital were due to this complication.

The end-results in this series of 570 cases were worked out for the years from 1922 to 1929 and were as follows (fractions are omitted):

| | Number | Death, Percentage | Cured, Arrested or Quiescent, Percentage | Alive and Improved, Percentage | Alive, Not Improved, Percentage | Untraced or Died of Other Causes, Percentage |
|---|---|---|---|---|---|---|
| Girls | 375 | 72 | 13 | 3 | 3 | 4 |
| Boys | 195 | 71 | 15 | 5 | 1 | 6 |

EUGENE SMITH, Ogden, Utah.

HISTOPATHOLOGIC PICTURE OF TUBERCULOUS MENINGO-ENCEPHALITIS. LAIGNEL-LAVASTINE and AMOUR F. LIBER, Encéphale **30**:77, 1935.

Three cases of diffuse tuberculous meningo-encephalitis in adults are reported. The free cells of the leptomeningeal infiltrate are classified as follows: (1) basal inflammation cells, lymphocytes, epithelioid cells, etc., which are generally arranged in diffuse sheets, not in follicles; (2) polygonal basophilic cells, which are mobilized fibroblasts and become granular cells, and (3) cells derived from the leptomeningeal covering, of which three types are distinguished—(*a*) large cytophages, (*b*) fusiform cells and (*c*) spongy pyriform cells. Transitional forms are found between these three types and between them and the covering cells. The latter are seen in different stages of mobilization and proliferation, both in the subarachnoid spaces and in the arachnoid villi. The epithelioid cells seem to be derived from monocytes. Giant cells, which are very rare, are of two types: (1) the usual foreign body type, associated with epithelioid cells, and (2) cells derived from vascular endothelium, not associated with epithelioid cells. The tubercle bacilli, which are very abundant, are found on the surface of the large cytophage cells, apparently without producing any necrosis. Bacilliform cell masses, composed of fusiform, pyriform and polygonal cells, undergo necrosis without going through the epithelioid or giant cell stages. The interstitial substances of the infiltrate are (1) a fine albuminous coagulum, (2) free connective tissue fibers and rarely (3) fibrin or fibrinoid substances. In one case, the dura presented zones of necrosis, with slight lymphoid infiltration and without bacilli.

LIBER, New York. [ARCH. NEUROL. & PSYCHIAT.]

THE HISTOPATHOLOGY OF TUBERCULOUS MENINGO-ENCEPHALITIS: II. THE NERVE PARENCHYMA. LAIGNEL-LAVASTINE and AMOUR F. LIBER, Encéphale **30**: 171, 1935.

Diffuse and circumscribed lesions were found mostly beneath the meninges and the ventricles. The neuroglia and the microglia presented proliferative and degenerative changes. A peculiar type of microglial reaction was transformation into forms resembling epithelioid cells. The neuroglia cells sometimes formed proliferative nodules. The ependyma presented hyperplastic foci, either pure or infiltrated with leukocytes and microglia cells, and zones of desquamation. The cells infiltrating the sheaths of the blood vessels were of the same type as those in the neighboring region of the meninges. They seemed not to be directly hematogenous but rather to invade the parenchyma from the meninges. In one case the vascular sheaths contained peculiar basophilic bodies and black pigment. Nodules of vascular origin did not present a follicular structure. The necrotic

center was invaded by reticular fibers. The walls of these nodules contained tubercle bacilli and seemed to be zones of extension. The stroma of the choroid plexus was infiltrated with lymphocytes and plasmocytes. Bacilli were found only in the meningovascular infiltrates, not in the neuroglia, microglia or ependymal formations or in the choroid plexus. The spinal nerve roots contained diffuse infiltrates and atypical nodules, which were rich in tubercle bacilli. From 5 to 10 per cent of the nerve fibers were degenerated. The lesions of the ganglion cells of the nerve centers were of diffuse and haphazard topography. The white matter was unaffected, save for small lacunae of disintegration about infiltrated vessels. The spinal ganglions were only slightly altered.

LIBER, New York. [ARCH. NEUROL. & PSYCHIAT.]

EFFECT OF ANTISYPHILITIC THERAPY ON THE TRANSMISSION OF SYPHILIS. A. TOURAINE and J. ROITENSTERN, Nourrisson **23**:363 (Nov.) 1935.

Statistics are given to prove that syphilitic mothers who have had antisyphilitic therapy have a much better chance of producing healthy babies than those who have had no such treatment. The best showing was made by those mothers who received their specific therapy during pregnancy. The modern methods of antisyphilitic treatment with mercury, arsenic and bismuth do not give results strikingly superior to the oral treatment of a generation ago with preparations of mercury and potassium iodide by mouth.

McCLELLAND, Cleveland.

TRANSMISSION OF SYPHILIS BY BLOOD TRANSFUSION. L. PÉRIN and M. LEFÈVRE, Nourrisson **23**:371 (Nov.) 1935.

A girl aged 2½ years acquired secondary syphilis two months after receiving a series of four blood transfusions from her mother. There were no stigmas of hereditary syphilis in the child. Inquiry revealed that the mother had contracted syphilis only a short time before she became a donor for the transfusions. Twenty similar tragedies have been reported in the French literature.

McCLELLAND, Cleveland.

VANADIUM IN THE PREVENTION OF CONGENITAL SYPHILIS. H. VIGNES and J. LEROUGE, Nourrisson **24**:152 (May) 1936.

In syphilitic pregnant women who cannot tolerate the usual treatments with arsenicals, mercury and bismuth, the authors report success with vanadium. A case in point is given in detail.

McCLELLAND, Cleveland.

CUTANEOUS REACTIONS TO TUBERCULOSIS IN CHILDREN FROM SIX TO TEN YEARS OF AGE. P. NOBÉCOURT and S. B. BRISKAS, Presse méd. **44**:913 (June 6) 1936.

Nobécourt and Briskas find that in the age groups from 6 to 10 years there is an augmentation of positive cutaneous reactions to tuberculin which is out of proportion to the relative fixity of the percentage of active tuberculosis. There is, however, during this period of four years, a passing increase in active tuberculosis in the eighth year in girls and the ninth year in boys. During the seventh year, the percentages of positive cutaneous reactions, of active tuberculosis and, to a lesser degree, of inactive disease are more elevated in girls than in boys. During the tenth year the percentages of positive cutaneous reactions, active and inactive diseases are essentially the same in both sexes.

BIEKER, St. Petersburg, Fla.

TUBERCULIZATION OF THE INFANT THROUGH AN EPHEMERAL CONTACT. A. VALLETTE and B. ROSENKRANZ, Rev. franç. de pédiat. **11**:192, 1935.

Two cases of tuberculosis in infants are reported in which, as far as could be determined, only a single brief contact with a tuberculous person had taken place.

LESLIE, Evanston, Ill.

PRACTICAL RESULTS OF THE SEARCH FOR TUBERCLE BACILLI IN THE GASTRIC CONTENTS OF CHILDREN. P. DE FONT-RÉAULX, Rev. méd.-sociale de l'enf. **4**:171 (May-June) 1936.

This paper analyzes the results described by Robert Debré and E. Lesné in their reports on the finding of tubercle bacilli in gastric contents of children who had an initial invasion by tubercle bacilli, erythema nodosum, tuberculous meningitis or even a positive skin reaction and no other sign of tuberculosis. The author speculates as a result on whether one should be more careful about isolating all children with a positive skin reaction from those with a negative reaction.

BROWNE, Detroit.

CHRONIC TUBERCULOUS JUVENILE MENINGO-ENCEPHALITIS WITH PUBERTAS PRAECOX, CHOKED DISK AND BITEMPORAL HEMIANOPIA. F. POOS, Klin. Monatsbl. f. Augenh. **95**:537 (Oct.) 1935.

Poos reports the case of a boy aged 12 whose father died from tuberculosis of the larynx and who had mutation of the voice and beginning puberty when he was 7 years old. He was apparently healthy to his eleventh year, when diabetes insipidus and polyuria developed, followed by visual disturbances and bitemporal hemianopia. His vision, which had decreased rapidly for two weeks prior to his admission to the hospital, disappeared after eleven days. The results of the ophthalmoscopic, neurologic and roentgen examinations and of the tapping of the spinal cord are given in detail. The boy died a few days after a trephination of the skull, which was done in a search for a cerebral tumor. Pathologic examination revealed caseous tuberculosis of the glands of the mesentery, chronic perihepatitis and perisplenitis. No cerebral tumor was found, but the brain substance was edematous, and edema was present in the chiasm, aside from granular ependymitis and papillary hypertrophy of the meninges near the pons. Encephalitis with granuloma and giant cells of Langhans' type was found histologically. The chronic intracranial tuberculous process, in Poos' opinion, was secondary to the mesenteric tuberculosis.

STOLL, Cincinnati. [ARCH. OPHTH.]

TRYPTOPHAN IN THE SPINAL FLUID IN TUBERCULOUS MENINGITIS. HARALD BOCK, Monatschr. f. Kinderh. **65**:41, 1936.

In every one of nineteen cases of tuberculous meningitis, tryptophan was found in the spinal fluid. In three cases of meningitis of nontuberculous origin also the test gave positive results. In ninety-seven cases of nontuberculous meningitis the test gave negative results. The writer expresses the belief that this test may be of value in differentiating tuberculous meningitis from nonsuppurative conditions, such as encephalitis.

GERSTLEY, Chicago.

CELLULAR STRUCTURE OF THE FOCAL REACTION IN TUBERCULOSIS IN COMPARISON WITH THE GENERAL AND LOCAL BLOOD PICTURE. H. BAAR, Acta pædiat. **18**:322, 1936.

Since it has become generally recognized that successive phases of many immunobiologic defense reactions are accompanied by an outpouring of different types of white blood cells, numerous efforts have been made to apply this knowledge to the clinical and experimental study of tuberculosis. Simpson, Sabin, Cunningham and Doan attach importance to the ratio between monocytes and lymphocytes in the circulating blood. Helmreich introduced the method of studying

morphologically the leukocytes obtained from an artificially produced cutaneous tuberculid (tuberculin test) in the hope of obtaining therefrom information regarding the cytologic composition of tuberculous foci situated in less accessible regions of the body. He applied this technic to the clinical evaluation of Ranke's classification of tuberculosis. Numerous objections have been raised against the clinical dependability of the method.

In order to obtain additional information concerning the correlation between the white cell contents of the blood, the experimentally produced tuberculid and the focal reaction, Baar injected from 0.1 to 0.5 mg. of old tuberculin into the pleural cavity in six patients suffering from tuberculous pleurisy and into the subarachnoid space in nineteen patients with tuberculous meningitis. A cell count of the pleural exudate or of the spinal fluid was made before, and from twenty-four to forty-eight hours after, this procedure. At the same time a count was made of the white cells in blood obtained from the finger-tip and of the white cells in a cutaneous papule (in this case, the Pirquet reaction).

In only a few cases was there any apparent correlation between the cellular formulas of the cutaneous papule and the spinal fluid. Baar states that the patients with tuberculous pleurisy had relative lymphocytosis in both the papule and the thoracic fluid; although the protocols support this statement in the literal sense of the word, the data are not convincing.

Baar leans heavily on hypotheses in arriving at the cautiously expressed conclusion that the cellular composition of the artificially produced tuberculous papule may provide some insight into the evolution of the internal tuberculous focus.

McCUNE, New York.

ABOUT THE DECREASE IN THE FREQUENCY OF TUBERCULOUS MENINGITIS. A. GUNTHER, Acta pædiat. **18**:340, 1936.

The researches of Langer and of Wallgren have demonstrated that tuberculous meningitis is particularly apt to supervene during the early stages of infection with the tubercle bacillus; the risk of invasion of the meninges diminishes appreciably after three months have passed from the time when the tuberculin test becomes positive. Wallgren has recently directed attention to the noteworthy decrease in the occurrence of tuberculous meningitis which has taken place in Gothenberg, Sweden. He has committed himself to the opinion that the credit for this improvement is due to the dispensaries for children which have been established throughout the community; he implies that the prophylactic activities of these agencies have been the most important factor in preventing the occurrence of meningitis in children who have already contracted tuberculosis. Gunther takes issue with this interpretation. A review of the situation in Gothenberg, Copenhagen, Oslo and Helsingfors reveals two additional factors which are of importance in explaining the decrease in the incidence of tuberculous meningitis. The first of these is the diminution in the number of cases of infectious tuberculosis which has taken place during the past twelve years; the second is the decline of the birth rate and the consequent decrease in the size of that portion of the population in which the incidence of tuberculous meningitis has always been highest. With no intent to disparage the value of the work of the dispensaries, Gunther suggests that many factors must be taken into account in explaining the lowered incidence of tuberculous meningitis in Gothenberg.

McCUNE, New York.

TIME OF MANIFESTATION OF TUBERCULOSIS OF BONES AND JOINTS. ARVID WALLGREN and ARTHUR LUNDBLOM, Nord. med. tidskr. **10**:1699 (Oct. 10) 1935.

In 113 cases of tuberculosis of the bones and joints the interval between the primary infection and the onset of signs in the bones was determined. It was found that in about 50 per cent of all cases this tuberculous disease manifested itself within one year after the primary infection, in more than three-fourths during the first two years, and in practically all during the first three years after infection.

In another series of 2,031 cases of tuberculosis of the bones and joints the age of the patient at the onset of the disease was noted. It was found that in most cases the lesions manifested themselves at from 6 to 30 years of age, with a maximum of frequency from 16 to 25. If this age curve is compared with a curve showing the percentage of fresh tuberculous infections occurring at different ages, a rather close similarity is found. This fact speaks in favor of the opinion that the great frequency of tuberculosis of the bone in later childhood, in adolescence and in young adult life depends on the greater frequency of primary infection at these age periods.

WALLGREN, Gothenburg, Sweden.

PULMONARY TUBERCULOSIS OF BOVINE ORIGIN. F. TOBIESEN, K. A. JENSEN and H. C. A. LASSEN, Ugesk. f. læger **97**:293, 1935.

Of 162 tuberculous children under 5 years of age, 7 had tubercle bacilli of bovine origin; of 105 children from 5 to 15 years of age, 6 had bovine tubercle bacilli. All the children had pulmonary changes, but the authors do not differentiate between the primary and the tertiary type of pulmonary tuberculosis. It is of interest to note that in 4 cases of erythema nodosum bovine tubercle bacilli were found (in 3 cases in the material obtained by lavage of the stomach, in the fourth case in the blood).

WALLGREN, Gothenburg, Sweden.

SENSITIVITY TO TUBERCULIN IN GLANDULAR TUBERCULOSIS OF THE NECK. P. BONNEVIE and T. K. WITH, Ugesk. f. læger **97**:893 (Aug. 29) 1935.

One hundred children and adults with tuberculous lymphoma of the neck were examined by means of graduated intracutaneous tests with tuberculin. The sign of a positive reaction with doses less than 0.01 mg. of tuberculin was an infiltrated area 4 mm. in diameter (with doses higher than 0.01 mg. the size of the area for a positive reaction was 5 mm.) on the fourth day. A negative reaction to 0.001 mg. of tuberculin or a negative Pirquet reaction proves that the lymphadenitis is not of tuberculous origin. The authors are of opinion that it is unnecessary in differential diagnosis to use larger doses than 0.01 mg. in order to exclude tuberculous etiology of a glandular swelling. In a series of forty-four patients they had only one who did not react to less than 0.1 mg.

WALLGREN, Gothenburg, Sweden.

## Diseases of Blood, Heart and Blood Vessels and Spleen

ROENTGENOLOGIC SKULL CHANGES IN THE ANEMIAS OF CHILDHOOD: REPORT OF A CASE; A FEW NOTES ON SIMILAR FINDINGS AMONG THE SKULLS OF PERUVIAN INDIANS. BENJAMIN F. FEINGOLD and JAMES T. CASE, Am. J. Roentgenol. **29**:194 (Feb.) 1933.

Erythroblastic anemia is characterized by definite changes of the bones. The changes in the skull, similar to those reported in sickle cell anemia, produce a thin or absent outer table, a thin inner table and a thickened diploe, which presents a striking picture. The long bones may also show pronounced changes in erythroblastic anemia. A case is cited of a Negro girl whose skull presented changes typical of erythroblastic anemia and sickle cell anemia, but there were no changes in the long bones and no normoblasts or sickle cells in the blood. The changes of the skull are indicative of a hemolytic process, but are not pathognomonic for either erythroblastic anemia or sickle cell anemia. Similar changes are shown by roentgenograms of the skulls of ancient Peruvian Indians. *Turmschädel*, or tower skull, is frequently described in association with hemolytic jaundice and results from hypoplasia of the base of the skull and secondarily from premature synostosis. The cranial tables are not involved, and the characteristic deformity is frequently considered pathognomonic of hemolytic icterus but should be used only as an adjunct to the diagnosis.

STULIK, Chicago.

DEXTROCARDIA IN CHILDREN. H. A. REISMAN, Ann. Int. Med. **10**:200 (Aug.) 1936.

The term "dextrocardia" as used in this article is employed to designate all conditions in which the heart is found in the right side of the thorax. Eight cases are reported. The etiologic factors responsible for the production of the condition in each instance are discussed.

READING, Galveston, Texas.

A COMPARISON OF HEMATOPOIESIS IN THE FETUS AND DURING RECOVERY FROM PERNICIOUS ANEMIA, TOGETHER WITH A CONSIDERATION OF THE RELATIONSHIP OF FETAL HEMATOPOIESIS TO MACROCYTIC ANEMIA OF PREGNANCY AND ANEMIA IN INFANTS. M. M. WINTROBE and H. B. SCHUMACKER JR., J. Clin. Investigation **14**:837 (Nov.) 1935.

Determinations of the number of erythrocytes per cubic millimeter, the mean corpuscular volume, the mean diameter and the proportion of nucleated red corpuscles and reticulocytes in the blood of fetuses and of new-born offspring of man, the pig, the rabbit and the rat led to the following conclusions: In each species, in young fetuses the number of erythrocytes is low and their size large when compared with the number and size of the red cells in the normal adult. As the fetus develops the erythrocyte count rises, the red corpuscles become smaller, and the proportion of nucleated red corpuscles and reticulocytes decreases. In all of the species examined some macrocytosis is still present at birth.

A comparison was made between the development of the blood in the fetus and the changes which occur in the blood of persons with pernicious anemia in response to liver therapy. In many respects the blood of the developing fetus resembles that of the patient with pernicious anemia who is being subjected continuously to an extremely potent stimulus to the formation of blood. It is suggested that the antianemic principle of Castle may be responsible for the described changes in the blood of the fetus and that this principle passes to the fetus from the stores of the mother. The significance of this concept in regard to anemia in newly born infants is discussed.

GUEST, Cincinnati.

PATHOLOGY OF SICKLE CELL ANEMIA. W. R. MATHEWS, New Orleans M. & S. J. **88**:671 (May) 1936.

In addition to presenting a good bibliography, Mathews reports the changes observed at autopsy in five cases of active sickle cell anemia and the pathologic changes in three spleens surgically removed in the course of the disease. The changes in the spleens indicate that some of the hemorrhages, showing both early and more advanced changes, are related to the rupture of overdistended pulp spaces.

It is suggested that the physical characteristics of the red cells in this condition offer an impediment to the circulation in the pulp spaces of the spleen and that a partial but sustained obstruction of this type may explain the stage of congestive splenic enlargement. Such a theory seems tenable.

BERKLEY, Los Angeles.

EXPERIMENTAL GOAT'S MILK ANEMIA. HOWARD L. ALT, Proc. Soc. Exper. Biol. & Med. **33**:48 (Oct.) 1935.

This study is based on the observation that infants fed goat's milk tend to acquire a pernicious anemia-like syndrome which responds to liver therapy but not to iron. White rats at weaning were fed goat's milk for sixty-five days. The erythrocytes increased from 6,800,000 to 9,500,000. The hemoglobin content decreased from 14 to 8 Gm. per hundred cubic centimeters. The number of reticulocytes rose, then dropped and then underwent a secondary rise. Severe anemia was developed by the method of Elvehjem and Kemmerer. The anemia produced in these experiments was similar to that produced by cow's milk. The animals were divided into three groups receiving: (1) iron and copper, (2) liver containing

the antipernicious anemia factor plus iron and (3) extract containing the hemoglobin-producing factor of Whipple. The response was the same in all groups and was similar to that found in the experiments with feeding cow's milk, the greatest response being due to iron and copper. HANSEN, Minneapolis.

TWO UNUSUAL CASES OF ANEMIA IN CHILDREN. L. L. LEE, South. M. J. **29**:504 (May) 1936.

The first case of anemia of an unusual type reported by Lee is one of acute hemolytic anemia (Lederer) in a 2½ year old girl. The symptoms were sudden onset, high fever, gastro-intestinal disturbance, extreme toxicity and jaundice. The most important symptoms and signs of the disease were (1) rapid hemolytic anemia, (2) marked hemoglobinuria, (3) moderate leukocytosis, with an absolute increase in neutrophilic polymorphonuclears and a moderate eosinophilia and (4) recovery after blood transfusion. Lee states that the etiology of acute hemolytic anemia is unknown but that it is undoubtedly a type of severe hemolytic anemia due to infection. One negative blood culture does not rule out infection.

The condition in the second case does not readily yield to classification as to type or etiology. The significant feature of the history was exclusive feeding with milk, with no vegetables, cereals or cod liver oil, but with some citrus fruit juices. The average red cell count was 900,000, with a low hemoglobin content (16 per cent) but a high color index, and the average diameter of the erythrocytes was 8.15 microns. The marrow of the sternum showed a decided decrease in the percentage of lymphocytes and an increase in the percentage of immature granulocytes. There was no leukocytosis, a slight leukopenia, and the differential count was about normal for a child of 6 years, except for a slight tendency to eosinophilia. The platelets, bleeding and coagulation time, fragility span and icteric index were all normal. While some features are atypical, there seems to be little doubt that the author was dealing with atypical deficiency anemia, most closely resembling that frequently seen in celiac disease or nontropical sprue.

SCHLUTZ, Chicago.

SPORADIC HEMOPHILIA WITH ESPECIAL REFERENCE TO SUCCESSFUL THERAPY. WILLIAM L. MARR and GEORGE HERRMANN, Texas State J. Med. **30**:494 (Dec.) 1934.

Two new sporadic cases of a different type of hemophilia are reported. The various methods of treatment of hemophilia are reviewed. It is believed that a reliable and effective treatment, constantly available, consisting of the intramuscular injection of whole blood taken from the patient himself, combines the effect of venesection with that of injection of blood.

The authors also believe from the results following the injection of whole blood that the decrease in the coagulation time can be explained on the basis of the increased platelet count, and it seems conceivable that these new platelets are less resistant to disintegration and therefore more likely to quicken the coagulation of the blood.

They also advocate a diet high in protein, gelatin and vitamin B between periods of bleeding, to promote the general health, prevent infection and maintain the clotting elements at the highest level.

The use of protein sensitization is effective if followed continuously, but care must be exercised not to produce a generalized reaction against protein. The latter is distinctly detrimental. It also seems that good results may be obtained in some cases by the use of female sex hormone. KNICKERBOCKER, Dallas, Texas.

ETIOLOGIC FACTORS IN A CASE OF HEMORRHAGIC PERICARDITIS. LÉON TIXIER and PIERRE BARDIN, Arch. de méd. d. enf. **38**:197 (April) 1935.

The authors report the case of a girl, aged 13, who was admitted to the hospital suffering from acute pain in the base of the left side of the chest, on

movement, together with slight dyspnea and a dry, unproductive cough. The patient had been ill for a month; there were malaise, a slight rise of temperature and marked loss of weight. In the second week a diagnosis of "grippe with cardiac development" was made, but the child continued to cough, and night sweats developed.

Examination revealed, in addition, immobility of the left side of the thorax, with pericardial dulness extending to the right of the sternum and 4 fingerbreadths below the normal apex point. The heart sounds were faint but normal; the pulse rate was regular, and the systolic pressure varied from 105 to 108. Roentgenograms demonstrated the usual features of pericarditis with effusion, which was confirmed by exploratory puncture and the withdrawal of fluid. This was bloody but did not coagulate. On standing it separated into two layers, the lower one resembling an ordinary blood clot and the upper composed of serum darker than normal in color. A portion of this evacuated fluid was injected into a guinea-pig. Four days later, paracentesis of this area gave entirely negative results and roentgenograms revealed pleural effusion on the left side.

After a further period of seven days the cardiac shadow was greatly diminished, and within a month all signs of the invasion had entirely disappeared; the patient was discharged recovered. The origin of the pericarditis remained obscure; such an effusion is much less common than serofibrinous or purulent exudates and is particularly rare in young subjects. It may be seen in scurvy, however, and also in yellow fever, purpura, icterus gravis and the hemorrhagic type of eruptive fevers. Cases have been reported in connection with acute articular rheumatism or pneumonia and in such chronic disorders as tuberculosis, cancer and Bright's disease.

In the case under discussion, all these factors could be eliminated except tuberculosis. In favor of such a diagnosis, the history showed that an aunt had died of tuberculosis; the patient had had an attack of measles and of whooping cough, which are known to be provocative; for a month prior to admission there were cough, night sweats and moderate fever; during the patient's stay in the hospital, pleurisy developed, and the skin reaction was positive. Against this hypothesis were the excellent general health of the child, the increase in the weight, the negative pulmonary findings with normal integrity of the tracheobronchial glands and negative results of inoculation.

AMESSE, Denver.

PURPURA TREATED WITH BLOOD TRANSFUSIONS AND INJECTIONS OF PEPTONE. MICHAEL CAMNER and MARIE CAMNER, Bull. Soc. de pédiat. de Iasi **6**:35 (April-June) 1935.

A child 4 years old showed numerous petechiae, a long bleeding time and a normal coagulation time but no retraction of the clot. The number of platelets was reduced to 30,000. Treatment with calcium chloride was of no benefit, and severe nosebleeds occurred. Injections of Witte's peptone given subcutaneously in combination with a small blood transfusion seemed to produce favorable results immediately. The blood became normal, and there was no recurrence of clinical symptoms. The authors do not believe that this might be one of those cases in which spontaneous improvement takes place.

LESLIE, Evanston, Ill.

VEGETATIVE ENDOCARDITIS AND SEPTICEMIA IN A YOUNG INFANT. P. LEREBOULLET, A. BOHN and J. ODINET, Nourrisson **24**:137 (May) 1936.

The disease occurred in an infant 3 months of age and ended fatally. The diagnosis was suspected during life and confirmed at necropsy. Attention is drawn to the difficulties in making an antemortem diagnosis. Although in some of the reported cases the disease was engrafted on a heart congenitally malformed, it was not in the case reported here.

MCCLELLAND, Cleveland.

HISTOPATHOLOGY OF THE EYEGROUND CHANGES IN NIEMANN-PICK'S LIPOIDOSIS. F. RINTELEN, Arch. f. Augenh. **109**:332, 1935.

The lipoids, which are ether-soluble and therefore fat-soluble, fall into three groups: phosphatides, cerebrosides and stearines. They are all essential components of living cells, and disturbances in their metabolism lead to certain well recognized disease entities, usually grouped together as the lipoidoses.

Four such diseases are recognized today: 1. A mild form of xanthomatosis, i. e., xanthelasma palpebrarum. This is due to a failure of the excretion of cholesterol, so that this alcohol and its esters are deposited in the different tissues, chiefly the skin. Here, as lipochrome, in characteristic cells tumor masses are found, with secondary reactive granulation tissue.

2. Schüller-Christian's disease. As a result of the deposition of stearines in the bones and meninges the following symptom complex arises: Through pressure of the xanthomatous nodes on the bones of the skull there develop the characteristic maplike markings and increased intracranial pressure with choked disk. Through pressure on the midbrain and hypophysis there develop diabetes insipidus and dystrophia adiposogenitalis. The growths in the orbit cause exophthalmos. As a rule the disease begins in childhood and runs a chronic course.

3. Gaucher's disease. In this disease there is a deposition of the cerebroside kerasin in the reticulo-endothelial system of the spleen, liver, lymph nodes and spinal cord. There are enlargement of the spleen and anemia, with hemorrhagic tendencies. The disease is often familial and has a preference for the Jewish race. Occasionally acute forms are seen, occurring usually in infants, with a predilection for the bones. Idiocy is often present as a result of lipoid degeneration of the cerebral ganglion cells.

4. Niemann-Pick's disease. Pick in 1922 differentiated the disease first described by Niemann as phosphatide splenohepatomegaly from Gaucher's disease. In this disease there is a deposition of phosphatides and, to a less extent, cholesterol in nearly all the organs. This is a disease of infants, nearly always of the Jewish race, and affects chiefly females. The liver, spleen and lymph nodes are enlarged. As a result of lipoid degeneration of the ganglion cells in the brain, flaccid and spastic paralyses develop, also progressive idiocy.

In seven of twenty-six patients examined the fundus resembled that in Tay-Sachs' disease in having a cherry-red spot in the macula. The analogy between the Niemann-Pick type of lipoidosis and Tay-Sachs' disease is so complete in many points that some authors regard Tay-Sachs' disease as a localized lipoidosis of the central nervous system (Bielschowsky). This is not accepted by other writers. Schaffer, for example, pointed out that in Tay-Sachs' disease the lipoid infiltration of the mesodermal elements characteristic of Niemann-Pick's disease has never been seen.

There are many points of difference between these two diseases, as Rintelen points out. There is neither splenohepatomegaly nor a characteristic blood picture in Tay-Sachs' disease. Familial occurrence is the exception. Further, Epstein was unable to find in Tay-Sachs' disease the increase in phosphatides in the brain which occurs in Niemann-Pick disease.

From a study of his case of Tay-Sachs' disease and Niemann-Pick's disease Rintelen draws the following conclusions:

1. The grayish green prominent ring seen around the red fovea in both these diseases can be explained by the following factors:

*(a)* Edema of the inner granular and inner reticular layers. This edema is caused by the toxic action of chemical products from degenerated cells. These cells are most numerous in the macular region; hence the edema is limited to this region.

*(b)* Lipoid infiltration of the ganglion cells in the macular region.

*(c)* An increase in the glial tissue.

2. The cherry-red spot is caused only by contrast between the normal fovea and the surrounding edematous macula.

3. The macular changes in Niemann-Pick's disease can be differentiated from those found in Tay-Sachs' disease histologically as follows: In the former disease there is no atrophy of the retinal nerve fibers and optic nerve, nor is there such marked lipoid degeneration of the ganglion cells.

4. The two diseases have sufficient points of difference to warrant keeping them separate as two distinct entities.

5. The cherry-red spot in the macula is not pathognomanic of any one disease entity but will always be found when there is necrosis of the ganglion cells with simultaneous fatty infiltration.

ADLER, Philadelphia. [ARCH. OPHTH.]

MYOCARDITIS IN YOUNG PERSONS, ESPECIALLY SCARLET FEVER MYOCARDITIS. E. STOEBER, Arch. f. Kinderh. **105**:193, 1935.

In agreement with the observations of earlier investigators Stoeber noted in the hearts of patients who died of scarlet fever various degrees of cell proliferation, partly perivascular and partly interstitial. These areas were filled with swollen fibrocytes, histiocytes, plasma cells and leukocytes. In the endocardium general dissemination of cells was noted, partly with cushion formation. Disintegrating processes within the cells or rheumatic nodules were not observed. One third of the patients examined showed no pathologic changes.

Comparison of the histologic changes of the hearts of patients with diphtheritic and rheumatic myocarditis with those in scarlet fever shows definite points of dissimilarity. Cellular infiltration and hemorrhage in the bundle of His is important as a cause of sudden death in scarlet fever. Agreement was observed between the pathologico-anatomic findings and the changes in conduction noted in the electrocardiogram.

CRANE, Chicago.

BREAST MILK AS A BLOOD COAGULANT. A. SOLÉ, Klin. Wchnschr. **14**:1354 (Sept. 21) 1935.

Solé reports that when a drop of fresh blood is placed on a slide and mixed with a drop of breast milk, the blood coagulates in from one and one-half to two minutes, whereas a mixture of blood with physiologic solution of sodium chloride coagulates in from five to ten minutes. The milk first becomes effective from fourteen to thirty days after lactation has begun and retains its effectiveness throughout the nursing period. The milk of febrile women is ineffective and cannot be used. There is no essential difference in the coagulating power of various samples of breast milk. Cow's milk and goat's milk do not seem to have this power. Breast milk will shorten the coagulation time of the blood of guinea-pigs, rabbits and dogs. The effectiveness of the milk seems to depend on the suspended particles of fat, and if the milk is centrifugated it loses its power. Fresh breast milk seems to be more effective than milk which has been pumped off and allowed to stand for some time. If the milk has not been tested, its effectiveness should be tried on a slide before it is used.

Breast milk has only a local coagulating effect on blood. Enteral or parenteral (intramuscular) administration has no influence. The author reports cases of hemophilia in which severe bleeding (following extraction of a tooth, cuts or nasal operations) was stopped by iodoform tampons soaked in breast milk.

ABT, Chicago.

INFECTIOUS MONONUCLEOSIS IN A BOY OF TEN. S. SALÉN, Nord. med. tidskr. **9**:591 (April 13) 1935.

The patient fell ill on Jan. 15, 1934, with general symptoms and fever and was admitted to a hospital with a diagnosis of leukemia. There were general enlargement of the superficial glands, hepatomegaly and a spleen that reached

the umbilicus. No jaundice or anemia was present. The white cell count was 12,500 (22 per cent polymorphonuclears and 78 per cent mononuclears). The polymorphonuclears were normal, but the monocytes consisted partly of ordinary lymphocytes, partly of a varying number of atypical cells, many of which could hardly be classified. The general condition of the boy was good. The fever subsided after ten days, and about a fortnight later the spleen and the liver were no longer palpable. He was discharged on Aug. 2, 1934.

WALLGREN, Gothenburg, Sweden.

## Diseases of Nose, Throat and Ear

RHINORRHEA IN CHILDREN WITH SPECIAL REFERENCE TO THE POSTTONSILLECTOMIZED CHILD. ABRAM H. PERSKY, Arch. Pediat. **53**:1 (Jan.) 1936.

Persky suggests lines of approach for those children in whom infection of the upper respiratory tract does not clear up after the removal of adenoids or tonsils.

WADDELL, University, Va.

CYTOPLASMIC INCLUSION BODIES IN THE HUMAN THROAT. JEAN BROADHURST, ROSAMOND M. LIMING, MARGARET ESTELLE MACLEAN and INEZ TAYLOR, J. Infect. Dis. **58**:134 (March-April) 1936.

The authors' summary is as follows:

"Cytoplasmic inclusion bodies may be demonstrated in human throats and other parts of the upper respiratory area.

"A relatively high proportion of persons with certain of the milder respiratory irritations are positive for these inclusion bodies.

"Carriers of these inclusion bodies may show an increasingly heavy incidence in the throat epithelial cells—both in the number of cells affected and in the number of bodies per cell.

"These inclusion bodies are rarely present in epithelial cells which contain bacteria.

"They are easily demonstrated in epithelial cells of affected persons; but they do not persist, in the same form at least, outside the host cells.

"These epithelial inclusion bodies seem acceptably classified as inclusion bodies: they multiply only when living tissue is available. They stain pink with Giemsa's stain (after Zenker's fluid). An aggregate structure (as in Negri bodies of rabies) and a capsule may be demonstrated by appropriate stains.

"Special stains have been developed for their ready differentiation from other cell parts and constituents and extraneous material: notably, nigrosinsodium chloride for throat specimens and methyl green—pyronin for embryo chick cultures. These cytoplasmic inclusion bodies have been cultivated in throats of monkeys and in embryo chick tissues."

TOOMEY, Cleveland.

CONTROL OF TONSIL AND ADENOID BLEEDING. LOUIS M. PEARLMAN, M. Rec. **143**:194 (March 4) 1936.

In the removal of tonsils and adenoids the surgeon meets with factors peculiar to bleeding from tonsils and adenoids: 1. It is difficult to see and to grasp the bleeding vessels because they are hidden by the soft palate and the anterior pillars and by the tongue. 2. The teeth constitute another barrier. 3. Blood may be swallowed for some time and remain unobserved until it is vomited. 4. The parts operated on cannot be placed entirely at rest. 5. The parts cannot be aseptically dressed. 6. A clot formed in the tonsillar fossa is prone to stimulate further bleeding by stretching the tonsillar fossa. A history of bleeding should make the physician take all the usual preventive measures before operation. Treatment should be instituted at once directly to the bleeding parts. Pearlman recommends

and discusses the following agents for stopping the bleeding: (1) a lamb's wool tampon, (2) artery clamps, (3) chemical cautery, (4) posture and (5) astringent drinks.

Reports on six cases conclude the article. WILLIAMSON, New Orleans.

BRAIN ABSCESS FOLLOWING ACUTE OTITIS MEDIA. E. WATSON-WILLIAMS, Brit. M. J. **2**:1152 (Dec. 14) 1935.

Watson-Williams gives a case report, the outline of which is included in the title.

ROYSTER, University, Va.

REMOVAL OF TONSILS BY ELECTRICAL CURRENTS OF HIGH FREQUENCY. ALBERT EIDINOW, Brit. M. J. **1**:152 (Jan. 25) 1936.

Eidinow's conclusions are as follows: "The application of high-frequency electrical currents, commonly called surgical diathermy, may be employed successfully to remove and destroy the diseased tonsil. The technique of progressive destruction by coagulation has advantages, since this operation can be performed while the patient continues with routine duties. The procedure is slow, involving treatment at weekly sessions for six to eight weeks. The discomfort and disturbance incurred by the patient is not really great, especially in suitable types of cases, but in the highly strung and nervous patient it causes apprehension and fear. However, I have managed to complete treatment in all the cases I have attempted, and no patient has, as yet, failed to complete treatment once he has agreed to start."

ROYSTER, University, Va.

PERITONSILLAR ABSCESS IN INFANCY. R. COMTY and M. SHUN-SHIN, Brit. M. J. **1**:1207 (June 13) 1936.

This is the report of a case of peritonsillar abscess in a child 2 months of age.

ROYSTER, University, Va.

OBSTRUCTIONS OF THE TRACHEA. L. COLLEDGE, J. Laryng. & Otol. **50**:897 (Dec.) 1935.

Colledge says that the causes of tracheal obstruction can be divided into (1) extrinsic lesions which cause compression of the trachea and (2) intrinsic diseases in the tracheal wall itself. In the first group are a large variety of conditions, such as mediastinal tumor, enlarged glands and aneurysm. The most common in this group are goiter and cancer of the esophagus. In the case of benign goiter the indication is clear: Enough of the goiter—whether in the neck or in the thorax—should be removed to relieve the pressure on the trachea. The real difficulty is presented by the dyspnea which is caused by malignant goiter and is often accompanied with paralysis of the vocal cords. The same often applies to esophageal cancer which gives rise to this kind of complication. In a case of malignant goiter, whether the cords are paralyzed or not, no attempt should be made to do a tracheotomy. Much the same applies to attempts to relieve the obstruction by König tubes, long flexible tubes which are intended to pass down through the obstruction. The trachea is so much covered by the growth that there will probably be the same trouble, although the plan is to open the trachea higher up. Crile suggested that relief may be obtained through decompression of the neck by dividing the sternothyroid and sternohyoid muscles, so that the tumor is allowed to expand outward. But often the malignant disease has invaded the muscles and they are so infiltrated and fixed by the growth that it is not likely that any large measure of relief is to be obtained in this way. After reviewing several cases, Colledge says that disease of the tracheal wall itself causes stenosis rarely. He mentions syphilis, tuberculosis and neoplasm. Syphilis occurring in this situation, apart from syphilis of the larynx, seems to respond well to anti-

syphilitic treatment, without leading to stenosis, as it is likely to do in the larynx if it is much advanced before treatment is begun. Tuberculosis of the trachea apart from tuberculous laryngitis is rare. In this connection he reviews an interesting case, describing the measures resorted to in order to overcome stenosis and obstruction. Primary tumor of the trachea is rare, but it is said that sarcoma is at least as common in this location as carcinoma. In these cases asthma is almost always diagnosed at first. The author reviews two cases in which this happened.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

OBSTRUCTIONS OF THE TRACHEA. F. C. ORMEROD, J. Laryng. & Otol. **50**:903 (Dec.) 1935.

Ormerod says that he was induced to make this report because in the museum of the Brompton Hospital there are examples of almost every type of tracheal obstruction. He does not include in this summary obstruction due to the inhalation of foreign bodies, and when this is eliminated, obstructions arising within the lumen of the trachea become few. There is, however, a specimen at Brompton Hospital of a pretracheal gland which became enlarged, eroded its way through the anterior wall of the trachea and fell down to the bifurcation, where it lodged. The patient got out of bed, fell on the floor and died. There have been several cases in which such a gland has lodged in a bronchus, but these do not come within the scope of the present discussion.

There are two main types of obstruction due to lesions arising in the wall: cicatricial stenoses and new growths. He mentions an instance of syphilitic structure, instances of stenosis following the wearing of a tracheotomy tube and one of stenosis following a bullet wound just below the larynx. Further, he describes a specimen of a trachea from a tuberculous patient. There are scarring and stenosis in the lower part of the trachea, which are assumed to be due to syphilis. There does not appear to be any real evidence as to the syphilitic nature, and the specimen belongs to the days before the Wassermann test was used. There are several similar specimens, all from tuberculous patients, but it is rare to find tuberculous lesions—particularly tuberculous stenosis—in the trachea. It is possible that the condition may be of syphilitic origin.

A new growth of the trachea may originate in the tracheal wall or may invade it from the thyroid and thymus glands, from the esophagus or from the upper lobe of the lungs, where it originates in a small bronchus and often reaches the lumen of the trachea by direct infiltration before it emerges from the main bronchus of the upper lobe. In the larynx one tumor is malignant to seven that are benign, but in the trachea the proportion is one to three. Symptoms of tumor in the trachea are dyspnea and a feeling of pressure behind the sternum or in the region of the larynx, according to the site of the lesion. There may be blood-stained sputum and stridor. The stridor is usually both inspiratory and expiratory, as opposed to the inspiratory stridor associated with laryngeal obstruction and the expiratory stridor that accompanies bronchial obstruction. The voice is affected only when the recurrent nerves are involved, and this involvement is surprisingly uncommon. Dysphagia is described as occurring when the esophagus is infiltrated, but probably the lesion often begins in the latter organ in such cases.

There are a number of cases in the recent literature of a tumor growing into the lumen of the trachea and probably originating in the wall. After citing several of these cases, the author says that obstruction of the trachea from causes arising outside is the most common type. Stenosis of the trachea from long pressure by an enlarged thyroid is common. After citing several cases from the literature, the author says that he had the opportunity of examining two patients with a similar condition with the bronchoscope. In one there was a fusiform aneurysm of the left common carotid artery pressing on the left wall of the trachea and causing a moderate degree of obstruction. In the other there was a saccular aneurysm of the arch of the aorta causing flattening of the trachea in an anteroposterior plane. The pulsation of the blood vessels was obvious in each instance. Both patients survived bronchoscopic examination and were able to return home.

Three other specimens from the Brompton Hospital are illustrated. One showed flattening of the trachea from behind forward by an enormous lymphoma of the mediastinal gland. A second showed stenosis of the lower part of the trachea due to endothelioma of the thymus. The third was that of a retrosternal goiter in a woman aged 59 who had severe dyspnea, but who made a complete recovery after removal of the thoracic portion of the thyroid gland. This patient's left recurrent nerve was paralyzed, and the condition was thought to be carcinoma, but histologic examination showed the growth to be a simple adenomatous goiter with degenerative changes. EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

THE MANAGEMENT OF OTITIS MEDIA AND SINUSITIS COMPLICATING THE COMMON COLD. LIONEL COLLEDGE, Practitioner **136**:33 (Jan.) 1936.

The management of suppurative otitis media calls for careful clinical observations. The common complications of meningitis, extradural or pernicious abscess and phlebitis of the lateral sinus, must always be kept in mind. Colledge points out that there are two forms of mastoiditis complicating acute suppurative otitis media. In one type the organism is a hemolytic streptococcus causing a thin discharge. The reaction is severe; localization usually does not take place, and septicemia is a real danger. Hence, early operation is indicated. In the second type of mastoiditis the discharge is usually a thick pus, the process is localized and operation after several days usually brings about good results.

Another complication of the common cold which is discussed is acute sinusitis. The author stresses the point that a minimum of surgical intervention is the best treatment of the patient. The danger of setting up acute spreading osteomyelitis in the facial or frontal regions is a real one. Several cases are reported to illustrate the discussion on acute sinusitis. SAPPINGTON, San Francisco.

A CASE OF AN IGNORED FOREIGN BODY IN THE TRACHEA. SUNE MEDAN, Paidoterapia **13**:793 (Oct.) 1934.

An instance of undiagnosed foreign body in the trachea of an 18 month old infant is reported. Because of the impression that the infant had pneumonia, the foreign body was overlooked on the first roentgenograms, which when later reviewed revealed its presence. The case proves the great advantage of direct laryngoscopic examination in children. HERRON, Spokane, Wash.

PULMONARY INVOLVEMENT AFTER TONSILLECTOMY. W. SCHÜTZ, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **139**:369, 1935.

Schütz says that Waldapfel, after his return from a trip to the United States, called attention to the higher incidence of pneumonia and of pulmonary abscess after tonsillectomy in America as compared with central Europe. This and the fact that the etiology of postoperative pulmonary complications was still in dispute induced him to review 403 cases of tonsillectomy with regard to the postoperative pulmonary complications. He was able to corroborate Waldapfel's assertion that the pulmonary complications after tonsillectomy are less frequent than in America, for he found pulmonary complications in only thirteen of these cases. He sees the cause for this difference from the American incidence in the technic of the intervention, particularly in the fact that in his clinic nearly all tonsillectomies are made with local anesthesia and never with ether anesthesia. In analyzing the incidence of postoperative pulmonary complications he found that the largest number were caused by the hematogenic dissemination of small emboli that had been liberated by the operations, and he applies the term "interstitial pneumonia" to the pulmonary complications that are produced in this manner. In three of the cases the complications could be traced to aspiration. In discussing the diagnosis of pulmonary complications he stresses the importance of the roentgenologic examination. EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

SPEECH DISTURBANCES IN CHILDREN AND THEIR CORRECTION. H. GUTZMANN, Gesundh. u. Erziehg. **48**:233 (Aug.) 1935.

Gutzmann discusses the various speech defects in children who have no anatomic deformities and no mental disturbance. These are stuttering, stammering, word deafness and disturbances of the voice. He stresses the importance of a complete history and thorough physical and mental examination, with an evaluation of the parental and environmental factors.

Psychotherapy and training are of importance. The methods already in use should be stopped; instead the parents should be given written instructions to follow. Special schools and classes are of value. Stammering is often due to organic changes. Thus, a thorough examination for defects should be undertaken. Word deafness may be difficult to identify, but one should suspect this when there is a delay in the time of talking. The use of a mirror is helpful in this type, but continued cooperation of the parents, instructor and child are essential. Disturbance of the voice itself is most frequently caused by so-called voice nodules. Excess crying may be responsible, and it is seen more commonly in urban than in country communities. Certain infections, such as tuberculosis, may also cause hoarseness. Harmonic vibrators and electromechanical tone control together with local therapy may be useful in this type of disturbance. The author believes that the earlier these various types of disturbance are treated the better the prognosis.

HANSEN, Minneapolis.

THERAPY OF DISTURBANCES OF SPEECH AND VOICE. H. STERN, Monatschr. f. Ohrenh. **69**:813 (July) 1935.

In the first part of his report Stern makes a few remarks regarding the treatment of lateral sigmatism. He points out that among the patients with this speech defect there are some in whom the proper position of the tongue and the proper direction of the air stream for the formation of the S sounds do not succeed in spite of all efforts. In such cases he urges the patient to bring his mouth into an exaggerated pipe position with indrawn buccal muscles. If this is done, the patient quickly gets the feeling for the proper direction of the air stream; at the same time the center of the tongue forms a groove and the lateral portion of the tongue, which was in the incorrect position, is brought away from that position and made to assume the right one. He points out further that the movements of the muscles of the face and mouth are usually more difficult and slower in persons who stutter than in normal persons. He says that rhythmic horizontal movements of the lower jaw during the process of phonation are well suited to improve this condition. This exercise, which he designates as *Kieferschütteln* (jaw shaking), although at first rather difficult for stuttering persons, produces a considerable improvement in their speech. Stern devotes the main portion of his report to the use of electric current in phoniatrics. He investigates whether and to what extent a better fixation of the larynx (with its favorable results) can be effected by treatment with electric current. In discussing the significance of the fixation of the larynx he stresses the importance of the hyoid bone and mentions the muscles that raise and those that depress the larynx. He shows that the depression of the larynx produces a number of favorable effects; it relieves tension, saves muscle powers, facilitates freer articulation, makes the vocal activity less labored and reduces the threshold of fatigue. He applies electrical stimulation to the muscles that depress the hyoid bone and the larynx, respectively, in order to effect fixation of the larynx in the optimal position and thereby exert a favorable effect on the voice production. After discussing the determination of the points of irritation on the muscles and nerves, the value of galvanic and of faradic current and the attachment of the electrodes, he points out that he combines electrical therapy with "internal singing," which involves a number of factors that aid and supplement one another in the depression of the larynx. He mentions (1) relieving the tension of the muscles that are active in raising the larynx, (2) keeping the larynx in the position of inspiration, (3) making adjusting movements before singing or speaking and (4) the so-called "covered mode" of

singing. He asserts that in suitable cases this form of combination therapy produces improvement in or even cure of vocal disturbances. He shows further that the determination of the conduction resistance can be used for diagnostic and differential diagnostic purposes. Finally he discusses the use of iontophoresis in phoniatrics.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

TUBEROUS HYPERTROPHY OF THE PALATINE TONSILS. S. ZOLTÁN, Monatschr. f. Ohrenh. **69**:864 (July) 1935.

Zoltán cites a few cases from the literature in which nodules the size of a pinhead or a peppercorn were found on the surface of hypertrophic tonsils, and then reports four cases of his own observation with the histologic changes. In evaluating his cases he emphasizes that his first case differed from the others in the histologic aspects. This case was one of a rare form of tuberculosis in which the productive process caused diffuse papillomatous hypertrophy of the surface of the tonsils. The histologic aspects in the other cases were different; on macroscopic inspection, the tonsils presented considerable similarity, but the histologic preparations showed differences. However, there was great hyperemia in all of them in spite of the fact that they appeared grayish white. This apparent contradiction can be explained by the edematous perfusion of the tissues. The edema in the epithelium covered up the original color of the organs and gave them an opaque appearance. Another common characteristic of the second group of cases was a deficiency in inflammatory processes. Most interesting was the behavior of the connective tissue. In some of the cases, the proliferation, loosening and hyaline sclerosis of the connective tissue dominated the histologic picture and were accompanied by atrophy of the lymph elements. Zoltán thinks that the apparent differences in the histologic aspects in the second group of cases can be explained by the differences in duration. He points out further that (according to one author) this second group includes also those cases in which hypertrophies develop on circumscribed parts of the tonsils, for instance, the so-called tonsillar polyps and accessory tonsils. In the last part of his report he makes suggestions regarding the possible course of the development and regarding the etiology of these tonsillar hypertrophies.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

OCCURRENCE OF STRIATED MUSCULATURE IN PALATINE TONSILS. L. HÖRBST and L. HASLHOFER, Monatschr. f. Ohrenh. **69**:927 (Aug.) 1935.

After citing other authors who observed striated muscle fibers in the tonsils, Hörbst and Halshofer describe their own observations on fifty-one tonsils from twenty-eight children. When both tonsils were available, usually one was sectioned parallel to the transverse axis. The authors observed striated musculature more or less far within the connective tissue septums of the tonsils from thirteen children. In most of these the musculature consisted of well preserved muscle bundles, oval on transverse section, whereas in several a few fibers lay loosely together, either stretched out or wavelike. The direction of these muscle tracts varied, for in the same section were sometimes both transverse and sloped ones. Although, in the majority, the musculature reached only to one fourth or to one third of the diameter of the tonsils, there were some in which the muscle bundles reached almost to the center. The authors show further that the connection of the intratonsillar muscular bundles with the musculature that adheres to the so-called tonsillar capsule cannot be denied. They call attention to connections between the base of the palatine tonsils and the pharyngopalatine and glossopalatine muscles, which in turn are girdled by fibers of the constrictor pharyngis; they point out that Glas saw in these connections of the palatine tonsils with the musculature of the constrictor pharyngis the cause for the appearance of muscular tissues in the tonsils. They show that this is the more understandable if the embryologic development of the tonsils is taken into consideration. They describe the embryologic development and reach the conclusion that in the arrangement and distribution of the muscular bundles there is a certain regularity, which is explained by the embryologic development of the tonsils.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

SHRINKING OF THE UVULA AFTER TONSILLECTOMY. K. BERNFELD, Monatschr. f. Ohrenh. **69**:932 (Aug.) 1935.

Bernfeld calls attention to a report on the fate of the uvula following tonsillectomy which was published by E. Fröschels (*Monatschr. f. Ohrenh.* **69**:155 [Feb.] 1935) and then describes his own observations. In study of about eight hundred uvulas he observed eight in which the shrinkage was severe, but he says that slighter changes in the volume were present. However, he observed not only shrinkage but, in two adults, swelling of the uvula. In discussing the causes of these changes he shows that the fate of the uvula is largely dependent on its involvement in the cicatrization after tonsillectomy. He stresses that among the patients showing severe uvular shrinkage he observed only one in whom the tonsillar niche was well preserved, whereas in the other seven he observed cicatrizations as well as more or less extensive obliteration of the tonsillar niche. Thus it appears that the shrinkage of the uvula can often be explained by mechanical factors in that the retracted uvula has been forced into the soft palate. As a second cause of the shrinkage, he considers the interruption of the lymph vessels and the obliteration of the blood vessels, as suggested by Fröschels. However, he remarks that this obliteration is probably the result not so much of a changed postoperative distribution of fluid in the uvula as of cicatricial traction. He thinks that the enlargement of the uvula observed in the presence of cicatrization and obliteration of the tonsillar niches after tonsillectomy indicates that the latter changes usually reduce the lymphatic stream and also cause obstruction and stasis in the uvula. A third possible cause of the shrinkage of the uvula considered by Bernfeld is the probable reduction of the lymphoid elements in the uvula following tonsillectomy.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

IODINE THERAPY IN OTORHINOLARYNGOLOGY. JOSEPH BERBERICH, München. med. Wchnschr. **83**:1678 (Oct. 9) 1936.

Berberich introduced the use of strontium salts for the roentgenologic visualization of arteries and veins. He found that strontium can supplant calcium as a therapeutic agent in many conditions, and its use avoids the unpleasant side actions following the intravenous administration of calcium, such as sensations of heat, malaise and vomiting. He then studied chemical combinations of iodine and strontium to be used in place of the various forms of iodine generally used for internal medication. Iodine is used in acute and chronic rhinitis, laryngitis, tracheitis and bronchitis. Because of the unpleasant side actions many physicians do not administer iodine. Berberich observed that strontium counteracts the undesirable effects of iodine as well as calcium does. For that reason he tried a combination of iodine, strontium and silicates in conditions requiring medication with iodine. The results were good, without the development of iodism.

BRAHDY, Mount Vernon, N. Y.

METASTASES IN OTOGENIC PYEMIA OF CHILDHOOD. IGNAZ HOFER, Wien. klin. Wchnschr. **49**:42 (Jan. 10) 1936.

Hofer states that if in the course of otogenic pyemia the symptoms persist even after the primary foci of infection have been treated, then the possibility of metastases must be considered. If there is local pain, the diagnosis is not difficult. Pulmonary metastases, abscesses and infarcts can be confirmed by roentgenograms, although there may be few symptoms. This may be the case when the metastases do not reach the pleura and there is no pleurisy. The prognosis of suppurative metastases in the hip joints, psoas muscle and pelvis is especially bad. Suppurative metastases in the hip joint usually do not remain confined to the joint but cause the formation of pus in the capsular ligament or inflammation of the bursa, which lies between the joint and the iliopsoas muscle, which may lead to continuation of the suppurative process in the fascia of this muscle, in the muscle itself and in the pelvis. Operative drainage of the pelvis is often difficult. The pus is retained, and there are attacks of severe fever and often hemorrhage. The child is weakened, and death often results from the suppurative process.

The treatment of metastases is usually operative, especially when other means remain ineffective. Cutaneous and superficial muscular abscesses may be treated conservatively or incised if they do not disappear. Individual pulmonary abscesses are curable. They may be coughed up or operated on by costal resection, especially if they have penetrated the pleural cavities and caused suppurative pleurisy. Metastases of joints which are small and near the surface may be treated conservatively. Larger joints may have to be punctured and drained.

Hofer's experience indicates that the formation of pus in the hip joint should be treated early by operative measures. In one of his cases of metastasis of the hip joint, however, the suppurative process reached the pelvis in spite of drainage and finally caused death. He expresses the belief that a more radical treatment might have been successful. In a second case there was spontaneous dislocation of the condyle, leading eventually to suppuration in the pelvis. Surgical removal of the necrosed bones and resection of the joint brought about a cure, although the bone was slightly shorter and the joint remained slightly stiff.

The author reports three other cases of metastasis. In each case there was localization of the process in only one part of the body: in the first patient, in the cerebrum; in the second, in the hip joint, and in the third, in the kidneys. The patient with metastatic abscess of the cerebrum could not be saved, although the abscess was incised. Operative treatment of the ear and of the hip joint saved the second child, and operation on the ear combined with internal treatment (intravenous injection and chemotherapy) saved the third. ABT, Chicago.

CONSERVATIVE TREATMENT OF PERFORATION IN OTITIS MEDIA. R. ZEIDLER, Wien. klin. Wchnschr. **49**:914 (July 17) 1936.

Zeidler has adapted an apparatus invented by Seidner, for use in the treatment of otitis media that has perforated. The apparatus consists of a double metal tube with two branches, an air pump worked by a jet of water, a stand with a container for medicaments and two rubber tubes. One wide branch of the double metal tube is connected with the pump, and the other branch, with the container. The pump, which can exert a suction equivalent to 76 cc. of mercury, can be mounted on a water faucet. The end of the metal tube which is opposite the branched end is placed in the ear of the patient after it has been covered with an appropriate perforated rubber plug. The pump is started, and the pressure within the ear is lowered. Through one branch of the tube the irrigating solution flows into the ear, and through the other branch it is sucked out. There is thus a continuous flow.

Over a thousand patients have been treated by this method. The first attempts were made on those with chronic otitis media and large perforations. Later the treatment was extended to those with acute disease and spontaneous or artificial perforations (paracenteses). Finally, all patients with nonoperative otitis media were treated. Of the more than a thousand patients, 21 per cent had acute otitis media. In most of these patients the treatment was strikingly successful. The pain disappeared immediately, and the temperature sank. Others required longer treatment (from two to four weeks, with three or four treatments a week).

Zeidler claims that this method of treatment provides adequate cleansing and drainage. It is not painful and not dangerous. There were no untoward incidents. The apparatus is inexpensive and easy to handle. ABT, Chicago.

PATHOGENESIS OF POSTANGINAL SEPSIS. S. NOZAWA, Ztschr. f. Laryng., Rhin., Otol. (Teil 1: Folia oto-laryng.) **26**:273 (Nov.) 1935.

Nozawa points out that there is still disagreement regarding the pathogenesis of postanginal sepsis. Some investigators maintain that phlebitis or thrombophlebitis in the region of the tonsillar veins is the focus of the septic process, whereas others are of the opinion that usually the process spreads first from the tonsils to the regional glands by way of the lymph channels and only secondarily by way of an infected thrombus that has developed beside a sup-

purating lymph node in the internal jugular vein. Those adhering to this second theory of pathogenesis consider primary thrombophlebitis of the tonsillar veins to be the exception. The author stresses that the clarification of the pathogenesis determines the therapeutic intervention, namely, the removal of the focus of infection. In order to gain a better insight into this problem he made experimental studies on young dogs. The animals were given intratonsillar injections of hemolytic streptococci or yellow staphylococci. Nearly all the animals died with signs of sepsis. They were subjected to careful examination, particularly of the oral, pharyngeal and cervical organs. Of the forty-five animals twenty-nine were selected in which pathologic changes were detected in the veins of the oropharyngeal or the cervical region. In all these cases there existed phlebitic or thrombophlebitic changes in the tonsillar root veins, but in fourteen cases the internal jugular vein was intact, whereas it was involved in the other fifteen. In eight of the fifteen cases just mentioned in which infection had been induced with streptococci the author demonstrated intravascular spread from the tonsillar root veins to the jugular vein. However, in the seven cases of this last group in which staphylococcic infection had been induced not only the internal jugular vein but the surrounding interstitial tissues and the adjoining lymph nodes showed severe destructive changes, so that it was impossible to determine definitely in what manner the jugular changes had developed. However, since in these seven cases the tonsillar root veins always showed pathologic changes, since these changes could be considered to be of primary periphlebitic nature and since, moreover, retrogressive spread of the process in the jugular vein could be excluded, it was assumed that in these cases the inflammation of the tonsillar root veins spread likewise by the intravascular path. The author reaches the conclusion that the phlebitis or thrombophlebitis of the tonsillar root veins is usually the primary process in cases of postanginal sepsis and that if the internal jugular vein becomes involved it does so usually by intravascular spread from the tonsillar root veins.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

A SIMPLE TREATMENT OF CROUP. HERMAN VON WILLEBRAND, Finska läk.-sällsk. handl. **78**:605 (Oct. 11) 1935.

Von Willebrand has treated croup with suction of the membranes by means of an electric vacuum cleaner armed with a rubber tube and a Nélaton catheter. If necessary, the suction can be combined with intubation. Twenty patients have been treated with this method of whom two with streptococcic laryngitis died.

WALLGREN, Gothenburg, Sweden.

## Diseases of Lungs, Pleura and Mediastinum

EXPOSURE TO COLD AS A FACTOR IN THE ETIOLOGY OF A LOBAR PNEUMONIA. A. J. NEDZEL, Illinois M. J. **68**:340 (Oct.) 1935.

From a review of his own experiments and those of others, Nedzel concludes that the presence of pneumococci in the upper respiratory tract is not a sufficient cause for the development of lobar pneumonia but that a dysfunction of the upper respiratory tract must precede the development of the pneumonia and this disturbance must be of such extent or type as to involve the whole respiratory tract and lead to the lowered resistance of certain tissues. This occurs when normal circulation of the blood is impaired. The vascular contraction of mucous membranes of the respiratory tract, which accompanies that of the skin during exposure, causes a delay in the mobilization of the defensive forces, and as a result of this disturbance in the irrigation of tissues they become impaired and the bacteria present find a favorable field for their development. The exposure of the body to cold is a powerful factor that not only causes the contraction of blood vessels of the skin but also, on account of the existing splanchnoperipheral balance, involves the blood vessels of the mucous membranes of the whole respira-

tory tract and causes stasis and edema in the lungs. If pneumococci are present, the lowered resistance of the whole respiratory system somehow permits the pneumococci to descend, lodge in the tissue of the lungs and multiply.

Exposure to cold acts as a powerful impulse and definitely upsets the splanchnoperipheral balance. The impulse causes the respiratory tract in toto to undergo physiologic changes which favor the penetration and localization of pneumococci or other organisms in the pulmonary tissue and permit their multiplication.

BARBOUR, Peoria, Ill.

BRONCHOSCOPY IN LUNG DISEASE WITH SPECIAL REFERENCE TO ATELECTASIS. CHARLES D. SNELLER, Illinois M. J. **69**:158 (Feb.) 1936.

After a defense of the bronchoscopist and a lengthy dissertation on indications for bronchoscopic examination, Sneller concludes that in all instances of protracted cough or expectoration in which tuberculosis has been ruled out, in all cases of obstructive atelectasis, in all cases of asthmatoid wheeze or similar "wheeze" and in all cases of dyspnea and cyanosis not proved to be due to heart disease, if bronchoscopic examination is carried out early, the physician will be better able to determine the cause and to treat atelectasis. In many cases pulmonary suppuration can be prevented in this way.

All of this, in the abstracter's opinion, is rather overdoing an enthusiastic effort to make physicians bronchoscopy minded. BARBOUR, Peoria, Ill.

BRONCHIAL ASTHMA: RESULTS OF TREATMENT IN TWO HUNDRED AND SEVEN PATIENTS UNDER OBSERVATION FOR A PERIOD VARYING FROM ONE TO THIRTEEN YEARS. LEON UNGER, J. Allergy **7**:364 (May) 1936.

This survey shows that in the majority of cases bronchial asthma results from extrinsic causes and begins in the first decade of life. It is in this group that the best results have been obtained. Approximately 20 per cent of the patients were free from symptoms for at least a year, 50 per cent were improved, 20 per cent were unimproved and 10 per cent were dead. Six died as a result of asthma.

Unger believes that asthmatic patients should be kept under observation for life because of a tendency to relapse. HOYER, Cincinnati.

THE PRIMARY PNEUMONIAS OF INFANTS AND CHILDREN. J. G. M. BULLOWA, Pub. Health Rep. **51**:1066 (Aug. 7) 1936.

Among 1,000 children with pneumonia there were 668 with lobar pneumonia and 331 with bronchopneumonia. However, bronchopneumonia occurred more frequently in infants and was more fatal in both infants and children. Nonpneumococcic pneumonias were more frequent and more fatal in infants than in older children. Infants are afflicted with pneumonia much more frequently than older children. A preponderance of cases of pneumonia was found among males, but no significant difference between the sexes in respect to mortality from pneumonia could be demonstrated. SANFORD, Chicago.

TOTAL PNEUMONECTOMY FOR BRONCHIECTASIS. R. WALKER, Proc. Roy. Soc. Med. **29**:212 (Jan.) 1936.

Walker reports total pneumonectomy on a boy of 7 years. At the age of 11 months he was admitted to the hospital with a history of cough for three months and difficulty with breathing for six weeks. Four months later he was admitted with bronchopneumonia in the lower lobe of the left lung. The next month he was admitted with a chronic cough, and he was reported to have consolidation of the lower lobe of the left lung. In December 1930 the tonsils and adenoids were removed. In February 1935 he was admitted to the hospital on account of pain in the left side and a cough following measles. From 1 to 4 ounces (30 to 120 cc.) of sputum with an offensive odor was coughed up daily. Clubbing

of the fingers was present. Roentgenograms of the chest taken a month later showed the left side of the chest to be completely opaque. The right lung was clear, and the heart was displaced a little to the left. At that time there were attacks of fever every few weeks, lasting a few days. Three months later injection of iodized poppy-seed oil showed bronchiectatic cavities in the upper and lower lobes of the left lung. Postural drainage yielded no improvement. Attempts at artificial pneumothorax were unsuccessful. Four months later a total lobectomy of the left lung was done. The patient was discharged from the hospital a month later, gaining weight. There was no cough or sputum. The last report was that he was able to run about without trouble.

WILLIAMSON, New Orleans.

BRONCHOPNEUMONIA IN INFANCY. EUGENIO CIENFUEGOS, Arch. de pediat., Rio de Janeiro **7**:165 (Jan.) 1936.

After a discussion of the types, complications and prognosis of bronchopneumonia, Cienfuegos concludes that the ultimate prognosis depends on the general state of the child and that there is no standard method of treatment. The general state of nutrition must be kept up, and complications should be met with treatment as they arise.

SANFORD, Chicago.

PLEUROPULMONARY SUPPURATIONS IN INFANTS. J. M. BARJAU MARTI, Paidoterapia **14**:601 (Nov.) 1935.

Barjau Marti stresses the great difficulties encountered in the differential diagnosis of pleuropulmonary suppurations and the importance of a rapid therapeutic intervention. He describes principally the acute tuberculous suppurations, describes empyema and abscess of the lung and presents a few cases of each.

HERRON, Spokane, Wash.

BLOOD TRANSFUSION IN EMPYEMA. MARTIN SCHLEGEL, Monatschr. f. Kinderh. **64**:329, 1936.

Schlegel gives case reports and roentgenograms of several children with empyema. In the treatment he found blood transfusion to be a valuable adjunct. Citrated blood was used in amounts of from 15 to 20 cc. per kilogram of body weight.

GERSTLEY, Chicago.

ASTHMA IN CHILDHOOD. LUDWIG HOFBAUER, Wien. klin. Wchnschr. **48**:1363 (Nov. 1) 1935.

Hofbauer states that asthmatic conditions in children are different from those of adults although the mechanism is the same, allergy being the principal cause of the respiratory disturbance. In adults the effect which the condition has on adjoining organs is different from that in children.

At all ages there are three groups of inciting causes: mechanical, secretory and toxic. In adults asthmatic conditions may often be caused by enlargement of the thyroid gland and disturbance of its secretion. In children disturbances of the secretion of the thymus or enlarged adenoid growth may cause difficulty in breathing. Enlargement of the thyroid gland and thymus may result in distortion and compression of the windpipe. In such cases one may be inclined to diagnose the difficulty as purely mechanical, but the disturbances of secretion may be much more significant. If the expiration is slow and difficult, the inspiration less slow and difficult, and there is audible stridor, the cause is usually mechanical. In asthmatic attacks caused by secretory disorders the expiration is deep and rapid, the respiratory excursions are variable, and there may even be pauses in breathing. Asthma from toxic causes (uremic asthma) may cause similar breathing.

If the respiratory tract is distorted, the stream of air may strike parts of the mucous membrane with undue force, remove warmth and moisture, and irritate the nerves. After operations for the removal of adenoid growths care should be taken that the physiologic type of breathing is restored. Often because of the postoperative stuffing of the nose the child becomes accustomed to a wrong type of breathing.

One must always keep in mind the possibility of asthmatic attacks due to the presence of foreign bodies. A foreign body may become lodged in the nasal passages and thus lead to mouth breathing. Or it may become lodged deeper in the bronchial tree. Often it may be of such nature that it does not give an adequate roentgenographic shadow. The formation of foci of atelectasis may aid in the localization.

So-called infectious asthma deserves special attention. In the sputum are found Haemophilus influenzae, Micrococcus catarrhalis or Micrococcus viridans. The patient should avoid any effort which increases the respiration; he should avoid talking. Steam from tea may be inhaled through the nose.

ABT, Chicago.

BRONCHOCOLONIC FISTULA. HELGA FELKL and ERICH MICHALEK, Wien. klin. Wchnschr. **49**:875 (July 10) 1936.

Felkl and Michalek report this condition in a boy of the age of 5 years and 9 months. In April 1933, he suffered from pneumonia of the left side with contraction of the left half of the thorax and formation of numerous bronchiectases. In March 1935, he had scarlet fever with consequent aggravation of the pulmonary condition. There was sacculated empyema in the diaphragmatic pleural cavity. The left sinus, especially anteriorly and laterally, was not affected. Six days later there was cessation of the pulmonary symptoms with onset of peritoneal symptoms in the left upper quadrant of the abdomen, indicative of penetration of the empyema through the diaphragm into the subphrenic region. After ten days the subphrenic abscess discharged into the eroded colon, as was made evident by the appearance of pus in the stools and the gradual subsidence of pain in the left upper quadrant of the abdomen. The puncture of the dilatated bronchial branch could hardly have taken place in the presence of the empyema, because this was not coughed up but penetrated into the subphrenic region. It is possible that the lower part of the fistula was caused by an infection ascending in the intestinal tract. The treatment of the condition was symptomatic and aimed at improvement of the general condition and avoidance of intercurrent infections. The possibility of extirpation of the lower lobe of the left lung and closure of the diaphragmatic puncture when the child was sufficiently well was considered.

ABT, Chicago.

CHYLOTHORAX IN CHILDHOOD. T. VARGA, Orvosi hetil. **79**:1021 (Sept. 21) 1935.

A boy 4 years of age acquired edema, with increasing weakness and dyspnea. The examination showed an exudation in the left side of the chest. The puncture gave 450 cm. of yellowish milky fluid. The microscopic examination showed only a few lymphocytes. Bacteriologic examination, culture and inoculation of animals gave negative results. At the place of the puncture a new exudation quickly developed. When the child was put on a fruit diet, the exudation cleared; when the ordinary diet was given, it again grew cloudy. Later an exudation started in the right side of the chest, but it soon ceased. The condition grew steadily better and the edema and the exudate diminished, so that he left the clinic three months later healthy.

Varga thinks that the chylothorax was caused by myocarditis, which caused stagnation of the blood.

GÖTTCHE, Budapest, Hungary.

## Diseases of the Gastro-Intestinal Tract, Liver and Peritoneum

IDIOPATHIC ULCERATIVE COLITIS IN CHILDREN. W. E. LADD and L. D. FOTHERGILL, M. Clin. North America **19**:1673 (March) 1936.

This condition occurs most commonly in early adult life, but the authors are here concerned only with the disease as it occurs in the first twelve years of life. Notwithstanding the numerous theories as to the causation, the etiology is still unsettled. The ulcerative process commonly involves the rectosigmoid and descending portions of the colon but may be more extensive. The ulcerations are small and placed close together, giving in the gross specimen a red granular appearance. As the disease progresses, the deeper layers of the colon are involved, with formation of scar tissue and at times peritonitis. The onset is usually insidious but may be abrupt. Gradually increasing looseness of the bowels with pain in the abdomen are the first symptoms. The stools are at first composed of mucus and later contain pus and blood. A low grade fever occurs in most cases. These symptoms may continue unabated or with remissions for months or years. The general nutritional condition becomes increasingly poor. Proctoscopic examination reveals the characteristic ulcerative basis of the disease. The most important conditions to be considered in differential diagnosis are amebic dysentery, tuberculous enteritis, chronic bacillary dysentery and rarely Meckel's diverticulum. When these have been eliminated, the choice of method in treatment will depend on the duration and severity of the disease. There is no specific medical treatment. General hygienic care, a low residue diet and antianemic therapy are indicated. The authors favor surgical treatment rather than prolonged persistence in medical measures. Transverse ileostomy with complete external diversion of the fecal stream will limit the progress of the disease and save the life of the patient who is rapidly going down hill.

EUGENE SMITH, Ogden, Utah.

ACUTE APPENDICITIS IN CHILDREN. PHILIP F. BARBOUR, South. M. J. **29**:500 (May) 1936.

When a diagnosis of acute appendicitis has been made one is faced with the problem of a prompt operation or symptomatic treatment. The decision will vary with the experience and judgment of the physician. If the condition is recognized early an operation offers the least risk. If the condition is catarrhal appendicitis and is not seen until some days have elapsed since the onset and if the general symptoms are clearing up, operation may be postponed and performed after an interval, with the minimum of risk.

SCHLUTZ, Chicago.

RECURRENT SWELLING OF THE PAROTID GLANDS. R. S. BRUCE PEARSON, Arch. Dis. Childhood **10**:363 (Oct.) 1935.

Eleven cases of recurrent swelling of the parotid gland are reported. These were characterized by the absence of evidence of infection and, in many instances, by a history of allergy. In three of the patients allergic manifestations frequently coincided with the development of the swellings. In one of these the passage of plugs containing large numbers of eosinophils from the parotid duct is described. It is suggested that these swellings may be allergic. The possible mechanism of the swellings is discussed. Obstruction of the ducts is thought to play a prominent part. Five cases in which there was evidence of infection are also described. It is suggested that infection may in some cases be superimposed on an allergic basis.

KELLY, Milwaukee.

HAEMORRHAGE PER RECTUM AS AN INDICATION OF DISEASE IN A MECKEL'S DIVERTICULUM. JUDSON T. CHESTERMAN, Brit. J. Surg. **23**:267 (Oct.) 1935.

Meckel's diverticulum is found in 2 per cent of persons. In 82½ per cent of these the diverticulum is lying free; in 10 per cent it has a free or attached band

at the apex; in 6 per cent it shows a fistula, and in the remaining 1½ per cent it shows some other abnormality. In pathologic conditions about five times as many males are affected as females, and in about 30 per cent of the cases the lesion occurs under the age of 3 years. Diseases occurring in the diverticulum may be classified as: inflammation, obstruction, fistula (either congenital or (acquired), neoplasms and associated local abnormalities.

About 80 cases of bleeding from the rectum caused by a Meckel's diverticulum have been reported in the literature to date. Etiologically, this hemorrhage might be due to ulceration of the peptic type and also might occur in cases of tuberculosis and typhoid fever. Ulceration of the base or apex is produced either through invagination of the apex or incipient intussusception of the base into the small bowel. Other causes of such hemorrhage are recurrent inflammation such as occurs in gastrostaxis, infarction and neoplasm.

The symptoms consist of hemorrhage from the bowel, anemia, pain, vomiting and irregularity of the bowel. Hemorrhage per rectum between the ages of 5 and 15 years, especially in boys, is suggestive.

The treatment is surgical. The mortality is 58 per cent in the cases in which perforation has occurred and 8 per cent in the cases in which perforation has not occurred.

Chesterman cites reports of four cases. SUMMERFELDT, Toronto, Canada.

CONGENITAL HYPERTROPHIC PYLORIC STENOSIS IN UNIOVULAR TWINS. J. W. REDGATE, Brit. M. J. **2**:725 (Oct. 19) 1935.

The condition reported is described in the title. The case is interesting, but offers nothing of special note. ROYSTER, University, Va.

VON GIERKE'S DISEASE ASSOCIATED WITH AMYLORRHOEA. A. E. NAISH and T. E. GUMPERT, Brit. M. J. **1**:360 (Feb. 22) 1936.

Naish and Gumpert give an exceedingly interesting case report, which must be read to be appreciated. It adds to the knowledge concerning this disease and possibly complicates the problem. ROYSTER, University, Va.

ACID DIARRHEA IN INFANTS. J. TAILLENS, Nourrisson **24**:134 (May) 1936.

The value of protein milk in the treatment of this type of diarrhea is emphasized. It acts by reducing fermentation and, on account of its low fat content, by lessening the quantity of fatty acids. The latter are believed to be especially irritating to the intestinal mucosa. MCCLELLAND, Cleveland.

FERMENTATIVE DIARRHEAS OF BREAST-FED INFANTS. JEAN CATHALA, Rev. méd.-sociale de l'enf. **4**:241 (July-Aug.) 1936.

The diarrheas of infancy are divided into: (1) alimentary diarrheas, due to (*a*) errors of routine, (*b*) hyperalimentation, (*c*) hypo-alimentation, (*d*) imperfect adaption of the digestive tract of the infant to the maternal milk; (2) infectious diarrheas, secondary to parenteral infections, and (3) constitutional diarrheas, often accompanied by disorders of the nervous system or skin. Cathala thinks that in none of these diarrheas is it necessary to wean the baby.

Increase in acidity and in fermentation of the stools is always present in diarrheas of breast-fed infants, owing chiefly to the fact that buffer substances (albumin and mineral salts) are low in woman's milk as compared with cow's milk and that lactose, the most easily fermented sugar, is high. Treatment consists, therefore, in neutralizing excessive fermentation and introducing into the digestive tract buffer substances, meanwhile quieting peristalsis by small doses of opiates. For these purposes are used purified animal charcoal albumin tannate, bismuth

salts, kaolin and precipitated calcium carbonate (especially recommended); camphorated tincture of opium or some other opiate, and occasionally replacement of part of the breast milk by cow's milk or the giving of a little calcium caseinate between breast feedings.

BROWNE, Detroit.

CONGENITAL ATRESIA OF THE ESOPHAGUS WITH TRACHEO-ESOPHAGEAL FISTULA. FELIX HURTADO, GUSTAVO CARDELLE and AMADOR GUERRA, Bol. Soc. cubana de pediat. **8**:67 (Feb.) 1936.

Hurtado, Cardelle and Guerra report a case of atresia of the esophagus with a tracheo-esophageal fistula. The malformation was situated at the level of the lower third of the esophagus.

The chief clinical symptoms were persistent vomiting of all fluids given and abundant foamy salivary excretion, the saliva running from the mouth and nose. In addition, the patient had a cough, frequent attacks of dyspnea and transitory cyanosis.

Roentgen examination confirmed the diagnosis.

A gastrostomy was performed, and the infant lived two weeks after the operation.

Bronchoscopic examination did not reveal the tracheo-esophageal fistula, but it was found at autopsy.

Injection of iodized poppy-seed oil post mortem revealed the condition in the roentgenogram.

SCHLUTZ, Chicago.

HYPERTROPHIC PYLORIC STENOSIS. JUAN DE DIOS UGARTE, Thesis, Bilbao, 1936.

Besides the usual signs and symptoms de Dios Ugarte thinks that roentgenograms are of value in the diagnosis of hypertrophic pyloric stenosis, since if a six hour retention is shown it is almost pathognomonic. Also a reduction of the plasma chlorides below 0.5 mg. per hundred cubic centimeters is significant. The modified Fredet-Ramstedt operation is the method of choice, and the mortality is practically nil. The bibliography with this article is the most complete that the abstracter has ever seen on this subject. Four hundred and fifty references are given.

SANFORD, Chicago.

INDICATION FOR OPERATIVE TREATMENT OF PYLOROSPASM. G. PASCHLAU and H. WILKE, Arch. f. Kinderh. **105**:167, 1935.

Roentgen examination of the stomach in combination with clinical observation makes it possible to differentiate pylorospasm which should be operated on immediately from that which can be treated conservatively. 1. If none of the contents has left the stomach after four or eight hours, immediate operation is absolutely necessary. 2. If after four hours less than one fourth and after eight hours less than one half of the contents of the stomach has passed into the intestine, immediate operation is likewise indicated. 3. If after four hours more than one fourth and after eight hours more than one half is in the intestine, conservative treatment may be tried. 4. If there is considerable emptying in the first four hours but little increase between four and eight hours, atonia of the stomach must be feared. Immediate operation is in order. 5. If the child does not gain or if he loses weight in from ten to fourteen days of conservative treatment, secondary operation is indicated.

Early or immediate operation is called for in the presence of a combination of pylorospasm and cardiospasm, of chronic atonia of the stomach, of coma pyloricum (after one or two days' treatment with sodium chloride) or of hydrolability with rapid loss of weight. Operation is contraindicated when there is acute dilatation of the stomach, toxicosis, decomposition, inflammation of the skin of the abdomen or acute infection.

AUTHORS' SUMMARY.

OPERATIVE TREATMENT OF CONGENITAL HEMOLYTIC JAUNDICE. R. WIPPERT, München. med. Wchnschr. **83**:928 (June 5) 1936.

A 16 year old girl had been jaundiced since the age of 3 years except for occasional jaundice-free intervals of several weeks. The spleen was barely palpable, the hemoglobin was 55 per cent of normal, and there were 2,330,000 red cells per cubic millimeter of blood. The indirect test for bilirubin showed 49 mg. per hundred cubic centimeters, and the direct test was negative. Splenectomy was performed. Two months later the hemoglobin was 88 per cent, there were 4,630,000 red cells, the direct van den Bergh test was negative and the indirect test showed between 0.3 and 0.37 mg., which are normal values. The patient gained weight and is greatly improved.

BRAHDY, Mount Vernon, N. Y.

TREATMENT OF APHTHOUS STOMATITIS. C. MONCORPS, München. med. Wchnschr. **83**:1647 (Oct. 2) 1936.

The first thing to do for aphthous stomatitis is to cleanse the mouth and throat thoroughly. Then removing tartar, filling cavities and treating chronic tonsillitis and other conditions are important. If local treatment with a 10 per cent sodium borate-glycerin compound or a 3 to 5 per cent tincture of iodine fails to have an effect, then foreign protein therapy should be tried. However, there are cases in which, in spite of any form of therapy, the condition recurs for some inexplicable reason.

BRAHDY, Mount Vernon, N. Y.

DIAPHRAGMATIC HERNIA IN A FOUR YEAR OLD CHILD. H. KUKOWA, Röentgenpraxis **8**:334 (May) 1936.

Kukowa reports the occurrence of a hernia on the left side.

MCCUNE, New York.

VARIABILITY OF INTESTINAL BACTERIA. A. REUSS and K. HASSMANN, Wien. klin. Wchnschr. **49**:769 (June 19) 1936.

Reuss and Hassmann note that the emphasis accorded to intestinal bacteria has been variously evaluated at different times. In the classic period of bacteriology these bacteria were looked on as the main cause of intestinal disturbances; in later times they lost this significance almost entirely. After a period they again received attention, and the fermentation they give rise to was considered one of the causes of intestinal irritation. The theory of internal infection of the small intestine was given recognition. But the division between alimentary and infectious disturbances persisted. A distinction was made between purely alimentary toxicoses and toxic illnesses caused by infection.

Some authors hold that under normal conditions there are pathogenic colon bacteria in the intestinal tract which have no effect on the healthy child because of an abundance of apathogenic organisms. Others hold that the pathogenic organisms come from an external source. It has been known for a long time that there are toxic colon strains, and they have been used to prepare antitoxic serums which are used with good effect in toxicoses of infants. A third possibility, which has not received much attention, is that the bacteria possess mutability, especially the colon group. In order to investigate this possibility, the authors made experiments at the Children's Clinic in Graz and at the Reichsanstalt of Vienna. An attempt was made to answer the question whether the digestive tract of the infant suffering from intestinal illness contains organisms which, like typhus and dysentery bacilli, do not ferment lactose and possess properties similar to the bacteria named. They are usually designated as paracolon bacilli. That these strains are relatively pathogenic is well known. Schubert and David recently reported a paracolon bacillus epidemic among soldiers who had eaten cheese. Most of them suffered from mild gastro-enteritis. If such cases are examined bacteriologically, the findings are usually negative, because only typhus, paratyphus and dysentery are considered in the differential diagnosis. Reuss recalls that during the war he

observed numerous persons who suffered from typhus or paratyphus and also patients who manifested similar clinical symptoms but yielded no positive bacteriologic findings. Reuss is now convinced that these cases belonged to the paracolon group.

Bacteriologic investigations made in the Children's Clinic at Graz showed that paracolon bacilli are frequently found in the intestinal tracts of infants, especially in those who suffer from severe dyspeptic or toxic disorders. Investigations carried on with the culture filtrates showed that the virulence of the bacteria varied considerably, though it was often very great. This was studied by intracutaneous injection in guinea-pigs, by the effect on the intestines of rabbits and by agglutination tests. The authors believe that in the intestinal tract colon bacilli degenerate into paracolon bacilli, leading to pathogenic and contagious modifications which, in turn, may become external sources of infection. They believe that the distinction between alimentary and infectious disorders of the intestinal tract must be given up. Infection with paracolon bacilli from external sources seems to be prevented by feeding with lactic acid milk. Whether internal degeneration of colon strains can be prevented by the same substance remains to be seen. Reuss and Hassmann believe that the variability of the bacilli has a much greater clinical significance than has been realized up to now. Lotze believes that the susceptibility of bacteria to external influences is of great importance in the genesis of epidemics. The authors hold that it is possible degeneration of streptococcic strains may be responsible for outbreaks of scarlet fever. The illness is often observed when there seems to be no possibility of infection from an external source. Similarly, cases of erysipelas are observed which cannot be accounted for by a consideration of external sources. Moreover, it is known that epidemics of disease vary in character and severity. Reuss and Hassmann believe this speaks for the possibility that modified bacilli cause the infection.

ABT, Chicago.

MEDICAL TREATMENT OF CONGENITAL PYLORIC STENOSIS. ELISABETH SVENSGAARD, Hospitalstid. **78**:833 (Aug. 13) 1935.

Reports are given of 179 cases (135 boys) of typical congenital pyloric stenosis, which were treated medically. During the period from 1911 to 1922 lavage of the stomach was rather frequently used and the infants were partially fed by means of a duodenal tube; 5 of 7.1 per cent of the 71 belonging to this group died. In the period from 1922 to 1927 treatment with atropine was begun; 3 infants, or 6.4 per cent, of 47 died. During the period from 1927 to 1934 atropine methyl nitrate was used instead of atropine, and 2, or 3.3 per cent, of the 61 infants thus treated died. In all three periods the children were fed with breast milk or with cow's milk mixtures, from 60 to 75 cc. per meal seven times a day. They were kept in isolation rooms, each with two beds.

WALLGREN, Gothenburg, Sweden.

CONGENITAL MEGACOLON. J. WANSCHER, Hospitalstid. **79**:596 (June 2) 1936.

Wanscher discusses the pathogenesis of congenital megacolon and describes the technic of resection of the presacral nerve. He reports the case of a patient who was rendered free from symptoms by nerve resection.

ELGHAMMER, Chicago.

LYMPHOSARCOMA IN A GIRL FIVE YEARS OF AGE. MOGENS NATHAN, Hospitalstid. **79**:620 (June 9) 1936.

This is a description of a case of lymphosarcoma in a girl 5 years of age and of the results of autopsy and microscopic examination. The tumor appears to have originated in the small intestine.

The position of lymphosarcomatosis in relation to tumors and blood dyscrasias is discussed. Special reference is made to lymphosarcoma in children, its occurrence and distribution in the intestinal canal, peculiarities of the pathologic anatomy, the symptoms and the treatment. Mention is made of favorable results obtained by radiation therapy in suitable cases. ELGHAMMER, Chicago.

A CASE OF ASCARIS INFESTATION OF THE ILEUS. HARALD HARPOTH, Ugesk. f. læger **97**:80, 1935.

A boy of 5 years fell ill with severe intermittent pains in the abdomen and mucosanguinolent stools. Sixteen hours later a tumor was felt in the left side of the abdomen and a roentgen examination gave evidence of obstruction, probably an intussusception. At the operation a number of ascarides were felt in the descending colon and the small intestines, but there was no tumor and no intussusception. The obstruction had disappeared. He was discharged in good health after having passed several parasites.

WALLGREN, Gothenburg, Sweden.

## Nervous Diseases

ABDOMINAL PAIN AS A MISLEADING SYMPTOM OF SPINAL CORD LESIONS. EVERETT D. KEIFER, Am. J. Digest. Dis. & Nutrition **2**:520 (Nov.) 1935.

Keifer relates that abdominal pain is often one of the early and outstanding symptoms of lesion of the spinal cord. Tumor of the spinal cord is not common, being considerably less frequent than intracranial tumor. The abdominal pain is caused by irritation of the posterior nerve roots. Many patients are operated on unnecessarily because the pain is referred to the region of the gallbladder, appendix or urogenital organs. Motor, reflex or sensory disturbances, although usually not marked, are frequently present.

The abdominal pain caused by spinal lesions often persists in a definite location over a long period. Frequently an increase in pain is produced by sneezing or coughing. Pain may be aggravated by any sudden change in the position of the body. Often there is associated pain in the lower part of the back or in the lower extremities or a girdle sensation about the trunk.

The author gives reports of cases, in two of which the patients were girls 15 and 17 years of age and in which abdominal pain was an outstanding symptom. It is interesting to note that chronic arachnoiditis was the cause of symptoms in these two cases and that laminectomy with freeing of adhesions produced a cure.

One should realize that the symptom of pain should be a factor in localizing the region of the tumor or disease of the spinal cord.

MORRISON, Savannah, Ga.

THE ELECTRO-ENCEPHALOGRAM IN EPILEPSY AND IN CONDITIONS OF IMPAIRED CONSCIOUSNESS. F. A. GIBBS, H. DAVIS and W. G. LENNOX, Arch. Neurol. & Psychiat. **34**:1133 (Dec.) 1935.

The electro-encephalogram was devised to record fluctuations in the electric potential that originates in the brain of human subjects. One electrode (a hypodermic needle) is inserted into the scalp at its vertex; the other is placed in the lobe of the left ear. For the study of grand mal epilepsy a special electrode was used. By this method standard curves were obtained and compared with those of patients having petit mal and grand mal epilepsy and other forms of unconsciousness. The procedure offers a new method for studying conditions in the brain, analogous to the electrocardiogram. BEVERLY, Chicago.

MESENCEPHALIC GLIOMA: A CLINICAL AND PATHOLOGIC ANALYSIS OF TEN CASES. BERNARD J. ALPERS and JAMES W. WATTS, Arch. Neurol. & Psychiat. **34**:1250 (Dec.) 1935.

Ten cases of mesencephalic glioma are reported. The clinical picture varies. In the more extensive of the tumors there is a combination of signs of involvement of the cranial nerves (chiefly oculomotor) of the cerebellum and motor and sensory disturbances. Choked disk may be present but is often absent. Objective signs of increased pressure are often pronounced, and the Argyll-Robertson pupil may be present. The course of the condition is downward despite operative intervention. Removal of the tumor is impossible.

BEVERLY, Chicago.

FAMILY PERIODIC PARALYSIS IN A GIRL AGED SEVENTEEN. J. A. BENDER, Arch. Neurol. & Psychiat. **35**:131 (Jan.) 1936.

A case of familial periodic paralysis of a girl is reported. The initial attack came on when she was 13 years of age, shortly after the second menstrual period. During the following two and one-half years she had eleven major attacks, lasting from twenty-four to seventy-two hours, and had persistent weakness of the legs, which was exaggerated about two days prior to menstruation. The case is of special interest, because there have been no major attacks during the twenty-eight months prior to the time of writing. The patient was given ovarian therapy, a 5 grain (0.324 Gm.) tablet of the dried residue of the whole gland, three times a day.

BEVERLY, Chicago.

ASYMMETRY: UNILATERAL ATROPHY AND FACIAL HYPERTROPHY. MABEL G. MASTEN, Arch. Neurol. & Psychiat. **35**:136 (Jan.) 1936.

Masten reports three cases of hemiatrophy. It is of special interest that the anomalies of development were associated with general physical and glandular inferiority. It is felt that in all three cases the asymmetry is to be regarded as the result of trophoneurosis due to embryonic defect in the visceral centers of the central nervous system.

BEVERLY, Chicago.

RELATIONSHIP BETWEEN THE PRESSURE IN THE VEINS ON THE NERVE HEAD AND THE CEREBROSPINAL FLUID PRESSURE. FREDERIC A. GIBBS, Arch. Neurol. & Psychiat. **35**:292 (Feb.) 1936.

Gibbs measured the venous pressure in the anterior chamber of the eyeball by inserting a hollow needle connected with a reservoir of physiologic solution of sodium chloride. Various pressures were compared with the cerebrospinal fluid pressure. He concludes: "When the cerebrospinal pressure exceeds the intra-ocular pressure and also the basic pressure in the veins on the nerve head, the pressure in these veins varies directly in an almost linear relationship with the cerebrospinal fluid pressure, until the level of the intra-ocular arterial pressure is reached."

BEVERLY, Chicago.

CEREBROSPINAL HYDRODYNAMICS: VII. EFFECTS OF THE INTRAVENOUS ADMINISTRATION OF HYPERTONIC SOLUTIONS OF DEXTROSE. JULES H. MASSERMAN, Arch. Neurol. & Psychiat. **35**:296 (Feb.) 1936.

The purpose of the study was to investigate the effect of the intravenous administration of hypertonic solutions of dextrose and the physiologic and semeiologic disturbances produced by the drainage of large amounts of cerebrospinal fluid.

Patients were given intravenous injections after the rapid drainage of the spinal fluid. It was found that intravenous administration of 500 cc. of a 35 per cent solution of dextrose causes a prolongation of the minimum period necessary for the restoration of the cerebrospinal fluid pressure to normal. It also increased the frequency and severity of postpuncture headache, backache, nausea, vertigo

and pyrexia. The administration of from 50 to 200 cc. of from 20 to 35 per cent solutions of dextrose has no determined influence on these functions. The administration caused no consistent effect on the pulse rate or the blood pressure.

BEVERLY, Chicago.

OBSERVATIONS ON FACTORS INHIBITING CHOREOATHETOSIS. W. O. KLINGMAN and E. R. CARLSON, Bull. Neurol. Inst. New York **5**:211 (Aug.) 1936.

Klingman and Carlson present clinical evidence to the effect that choreoathetosis as a result of injuries sustained at birth or other conditions may have its origin in the higher centers of the cortex. These movements are markedly reduced following ether anesthesia, strong emotional experiences, cortical trauma or an intake of alcohol.

BEVERLY, Chicago.

THE SYNDROME OF THE UNRUPTURED ANEURYSM OF THE INTRACRANIAL PORTION OF THE INTERNAL CAROTID ARTERY. J. M. MCKINNEY, T. ACHREE and S. E. SOLTZ, Bull. Neurol. Inst. New York **5**:247 (Aug.) 1936.

The authors have reviewed eight cases and collected reports of twenty-nine from the literature. They conclude that the classic syndrome of an unruptured aneurysm of the intracranial portion of the internal carotid artery consists of exophthalmos and partial or complete involvement of the second, third, fourth, fifth and sixth cranial nerves on the side on which the aneurysm exists. The third and fifth cranial nerves are always involved, and the others usually. Exophthalmos was present in five of eight cases.

BEVERLY, Chicago.

PROBLEMS OF THE ACUTE INFECTIONS OF THE CENTRAL NERVOUS SYSTEM. J. B. Neal, Bull. Neurol. Inst. New York **5**:278 (Aug.) 1936.

This article presents an excellent summary of the present status of knowledge of the causes, diagnosis and treatment of meningitis, poliomyelitis and encephalitis. An adequate summary cannot be made; the article should be read as a whole.

BEVERLY, Chicago.

LATERAL SINUS THROMBOSIS. N. O. EADDY, J. South Carolina M. A. **32**:4 (Jan.) 1936.

The importance of this condition is brought to the attention of rural and general practitioners chiefly. Lateral sinus thrombosis is not an uncommon condition. This disease is usually secondary to infection of the middle ear. A textbook discussion is undertaken. A number of case histories are reported.

WESTON, Columbia, S. C.

VARIATIONS IN PLASMA MAGNESIUM AND POTASSIUM IN EPILEPSY. ARTHUR D. HIRSCHFELDER and VICTOR G. HAURY, Proc. Soc. Exper. Biol. & Med. **33**: 40 (Oct.) 1935.

Low magnesium and high potassium values in the plasma, with a high potassium-magnesium ratio, were found in a series of epileptic subjects. The more severe the seizures, as in status epilepticus, and the more frequent the occurrence of the convulsions, the more marked these findings were. The value for plasma calcium was always within normal limits. For seventeen patients with epilepsy who were not having convulsions, the values for plasma magnesium, potassium and calcium were normal. Magnesium chloride administered orally did not lessen the frequency of seizures, nor did potassium chloride decrease the frequency of the seizures.

HANSEN, Minneapolis.

A Review, Clinical and Pathological, of Parahypophyseal Lesions. Charles H. Frazier, Surg., Gynec. & Obst. **62**:1 (Jan.) 1936.

Tumors of the brain which may arise in the region of the sella are divided into eight types: (1) intracranial aneurysm, (2) tumor of the optic chiasm, (3) tumor of the sphenoidal ridge, (4) pseudotumor, (5) tumor of Rathke's cleft, (6) tumor of the hypophysial stalk, (7) suprasellar fibroblastoma, (8) suprasellar adenoma. The tumors found especially in children are of types 2 and 6.

A globular tumor, almost always a glioma, is found occasionally, involving one or both optic nerves alone or with the chiasm. The diagnosis is speculative unless by the roentgenogram one finds the optic foramina enlarged and the anterior section of the sella turcica expanded forward. Primary atrophy of the optic nerve and defects of the visual field are inevitably associated with loss of visual acuity.

The most common of the parasellar tumors found in children are those of the hypophysial stalk. Symptoms may be present for months (from four to ten) or for years (from one to seven). The basal metabolic rate is always subnormal. Primary atrophy of the optic nerve or papilledema with secondary atrophy of the optic nerve is present. The visual fields usually show a temporal or bitemporal hemianopsia; but binasal or homonymous hemianopia, concentric contraction and other types may be found.

Because of the pressure of the tumor of the hypophysial stalk on the hypophysis, endocrine disturbances of one kind or another form part of the clinical picture. In order of frequency these are dwarfism, somnolence, adiposity, sexual defects, femininity, polyuria, amenorrhea and emaciation. Generally speaking, the endocrine features are those of the Fröhlich type.

The usual signs of increased intracranial pressure may be present, such as headache, vomiting and papilledema. In a few instances there are associated or neighborhood symptoms, such as visual or auditory hallucination, deafness, tinnitus, vertigo and diplopia. The roentgenogram may show the sella turcica to be enlarged, or atrophy of the dorsum sellae may exist. The most significant roentgen evidence, as concerns the differential diagnosis, is calcification. In half the cases reported calcification was present.

This combination of shadows of calcified areas in the roentgenogram, endocrine disturbances, and disturbances of the fields of vision, with alterations in the disks, especially in young persons, bespeaks with reasonable certainty a tumor of the hypophysial stalk.

Histologically the tumor is characterized especially by a basilar layer of ameloblastic cells. The tumor is likely to undergo cystic degeneration, with numerous areas of calcification.

Budson, Detroit.

Encephalography in the Investigation of Certain Cerebral Conditions in Childhood: II. Arch. Dis. Childhood **11**:97 (June) 1936.

The technic of encephalography was described in the previous paper. In this paper forty-seven cases in which encephalography was used as an additional method of investigation are presented. There are twenty-four excellent encephalograms with descriptions of the principal forms of cerebral defects encountered in the investigation.

Kelly, Milwaukee.

Intramedullary Abscess Causing Spinal Compression and Meningitis. A. G. Maitland-Jones, Proc. Roy. Soc. Med. **29**:215 (Jan.) 1936.

A girl 2½ years old had been well until four days previous to her admission to the hospital, since which time she had lost the use of her legs and had been fretful. On examination she was feverish, with rigidity of the neck and back and complete flaccid palsy of both lower limbs with sensory loss to the level of the eighth thoracic vertebrae. There was also incontinence of urine and feces. The cerebrospinal fluid showed 580 cells (90 per cent finely granular oxyphils). The protein content was 4.8 per cent, and a culture was sterile. The fever and meningeal signs lasted for ten days, and the stiffness of the back continued for

about four weeks. A roentgenogram of the spine showed no abnormality. The Mantoux test gave negative results. Iodized poppy-seed oil introduced into the lumbar theca was found by roentgen examination to be arrested at the lower border of the ninth thoracic vertebra when the patient was inverted. The cord was exposed over this area by operation, and the dura was found to be thickened and adherent to the cord. There was no pulsation at or below this part. The cord was enlarged and with a needle and syringe 0.5 cc. of yellow fluid was removed. The fluid contained large cells resembling epithelial cells. The nuclei of many were degenerate, and the cytoplasm of most contained droplets staining red with scarlet red. The child contracted pneumonia after the operation but recovered in a few days.

WILLIAMSON, New Orleans.

ENCEPHALITIS WITH APHASIA IN A BOY OF TWELVE YEARS. RADERMECKER, Arch. méd. belges **88**:165 (July) 1935.

The patient was an intelligent boy advanced in his school work, who suddenly had a series of epileptic attacks culminating in a high fever for three days, with complete right hemiparesis. Some days later loss of speech was observed. He understood all that was said to him. He could speak only in monosyllables and had forgotten how to say his prayers. He could not read or understand printed text. He could not write anything but his name. There was no vomiting, headache, nuchal stiffness or other sign of meningitis. The pupil of the left eye was edematous and appeared slightly atrophied; both papillae were surrounded by pigmented halos. The neurologic examination revealed no further points of interest. The Kahn reaction was doubtful; that to colloidal benzoin was distinctly positive. The patient was put on antisyphilitic treatment and made rapid improvement.

VINTON, New York.

ROENTGENOLOGIC DIAGNOSIS OF HYDROCEPHALUS IN UTERO. P. BRAULT, A. TIZON and PICOT, Bull. Soc. d'obst. et de gynéc. **24**:435 (July) 1935.

The case reported is that of a primipara delivered at term after an uneventful pregnancy. After rupture of the membranes a breech presentation was diagnosed, and the patient was admitted to a hospital. More complete examination with the patient under an anesthetic showed that not a breech but a large head was presenting. As the patient had a contracted pelvis, a roentgenogram was made to determine whether it was a large fetus with a large head or a hydrocephalic infant. The roentgen diagnosis was hydrocephalus, with the skull so well ossified that it would be extremely difficult to deliver, even if perforated and reduced. A low cesarean section was done, and a living hydrocephalic girl was delivered. The hydrocephalus was progressive and resisted all operative measures. The child was living and gaining weight when seen at the age of 3 months. The authors point out the misfortune of the child's survival but do not think that the obstetrician can be criticized for refusing to kill a living infant in utero, even if it has hydrocephalus.

GLASER, Rochester, N. Y.

PATHOGENESIS OF SYRINGOMYELIA: CLINICOPATHOLOGIC STUDY OF ONE CASE. R. BURDET and F. E. POSTHUMUS MEYJES, Encéphale **30**:137, 1935.

In a child aged 6 years atypical symptoms had been diagnosed as psychoneurotic by several pediatricians. Examination showed paresis of both upper limbs, ankle clonus and rigidity of the neck. The roentgen findings were normal. Examination of the spinal fluid showed a positive reaction to the Nonne-Apelt test, 20 lymphocytes, no micro-organisms and a negative Wassermann reaction. Iodized poppy-seed oil was arrested at the level of the first thoracic vertebra. The child died of acute bronchopneumonia before an operation could be performed. Autopsy showed two intraspinal tumors at the level of the fourth cervical vertebra, histologically resembling medulloblastoma. Between these tumors a column of glial tissue occupied the dorsal funiculus. It contained a syringomyelic cavity, distinct from the central canal, surrounded by small round glia nuclei, elongated

nuclei of connective tissue type, abundant mesenchymatous fibers and iron pigment. A diffuse inflammatory process, consisting of lymphoplasmocyte perivascular muffs, was most marked in the ventral horns and at the limits of the pathologic tissue. The dorsal vagus nuclei were atrophied and "flattened" by distention of the fourth ventricle, which explained the absence of a reflex cough during the bronchopneumonia and the persistence of the voluntary cough.

LIBER, New York. [ARCH. NEUROL. & PSYCHIAT.]

PATHOGENIC RÔLE OF ENDOCRINE DISTURBANCES IN EPILEPSY. J. S. RABINOVITCH, Encéphale **30**:350, 1935.

In a clinical and biochemical study of thirty-four epileptic patients Rabinovitch observed that epileptic seizures occur particularly during menstruation and in persons with amenorrhea often at the date of the expected period. The blood sugar curve during fasting is polymorphous and labile. The blood sugar content often drops to 40 mg. per hundred cubic centimeters or even lower two hours after the ingestion of dextrose. Hypoglycemic curves occur in cases of all types of epilepsy but more particularly in cases of petit mal and psychic equivalents and in those in which the patient presents the heredofamilial history described by Bratz: left-handedness, stammering, enuresis and epilepsy. The hypoglycemic phase alone is, however, insufficient to provoke an attack. The basal metabolic rate is generally normal. Its variations are not correlated with the frequency or intensity of the epileptic seizures. In one epileptic patient suffering from exophthalmic goiter, thyroidectomy was followed by a lowering of the basal metabolic rate without any change in the rhythm of the attacks. In most cases a slight lowering of the alkali reserve and slight hypercalcemia were found.

In general, the endocrine and vegetative systems are very unstable, although epilepsy is not as a rule associated with any frank endocrinopathy. No endocrine condition can result in epilepsy without concomitant lesions of the nervous system. According to Buscaino's expression, in all epilepsy there are a cerebropathy and a biopathy. In view of the researches of Frisch and others showing that retention of water is a factor in the production of the seizure, Rabinovitch expresses the belief that endocrine and vegetative disturbances exert their influence by producing retention of water. He rejects the classic concept that the sympathetic nervous system and the glands innervated by it are epileptogenous, while the vagus nerve and the glands innervated by it are antiepileptic. A notable incongruity of this schema is the necessary inclusion in the vagus group of the pancreas, the excessive functioning of which is known to be epileptogenous. From the water retention hypothesis, Rabinovitch derives the following schema:

| Glands which oppose epileptic manifestations | Glands which favor epileptic manifestations |
|---|---|
| 1. Adrenals | 1. The Langerhans apparatus of the pancreas |
| 2. Thyroid | 2. Posterior lobe of the hypophysis |
| 3. Parathyroids | 3. Persistent thymus |
| 4. Anterior lobe of hypophysis | 4. Epiphysis (?) |
| 5. Genital glands | 5. Corpus luteum (??) |

LIBER, New York. [ARCH. NEUROL. & PSYCHIAT.]

THE TREATMENT OF SYDENHAM'S CHOREA BY INTRAMUSCULAR INJECTIONS OF MAGNESIUM SULFATE. MARIN RAMOS CONTRERAS, Presse méd. **44**:228 (Feb. 8) 1936.

Contreras believes that intramuscular injection of magnesium sulfate is the treatment of choice for chorea. The advantages are: the ease of administration, the almost immediate amelioration of symptoms and the freedom from undesirable after-effects. He gives a deep injection of a 25 per cent solution every two days—

5 cc. to children under 5 years of age and 10 cc. to older children. This is not sufficient to produce somnolence, and, aside from some soreness at the point of injection, no untoward effects are produced.

Five cases are reported. In all these, cessation of symptoms was shown after eight to ten injections. In two cases, concomitant cardiac symptoms also disappeared.

The exact mode of action of the magnesium sulfate is not clear. It is apparently not hypnotic, since the dosage is insufficient for this and since other powerful hypnotics, namely, the barbiturates, are ineffective. Stimulation of cerebral circulation with consequent resorption of cerebral edema may explain some of the effect. Perhaps magnesium, which is an element present in nerve tissue, is more concerned than other salts in osmotic change. The cure of the cardiac complications in two cases, however, is strongly suggestive of specific action on the unknown bacterial cause of chorea.

BIEKER, St. Petersburg, Fla.

THE TREATMENT OF PARALYSIS BY THE PUTTI OPERATION. JULIO MARTÍNEZ and MANUEL MIRANDA, Arch. de med. inf. **4**:238 (Dec.) 1935.

Martínez and Miranda used a modified form of the Putti operation for the orthopedic treatment of paralysis in two cases. They state that two cases are not enough on which base any definite claims, but certainly the results in these two were excellent. The method is described in full.

SANFORD, Chicago.

GLIOMA OF THE CEREBELLAR VERMIS. ROGELIO CHARLONE and M. L. SALDÚN DE RODRÍGUEZ, Arch. de pediat. d. Uruguay **7**:398 (Sept.) 1935.

Charlone and Saldún de Rodríguez report this pathologic condition in a child aged 3 years. Early symptoms were flexion and slight rotation of the head, with torticollis. These symptoms followed an acute febrile attack and bilateral purulent otitis media, which had developed two months previously. Cephalalgia, vomiting and difficulty of gait then developed. There were horizontal nystagmus, incoordinate movement of the extremities, wide separation of the cranial sutures and progressive increase of all the cerebellar symptoms. Decompression and ventricular puncture gave no relief. At autopsy a glioma of the cerebellar vermis was found.

SCHLUTZ, Chicago.

ACUTE INFECTIONS OF THE NERVOUS SYSTEM IN A CHILD. EUCLIDES PELUFFO, Arch. de pediat. d. Uruguay **7**:49 (Feb.) 1936.

Many of the obscure acute nervous syndromes in childhood are often linked to acute cutaneous infection. Peluffo presents a report of four such cases.

Complex neurologic pictures with variable symptoms and with progressive paralytic manifestations were present. The immediate prognosis in these conditions is grave, owing largely to inability to check the progressive extension of the process and to the appearance of bulbar paralysis.

If the patient does recover, regression of all symptoms takes place and complete recovery without any sequelae is assured.

SCHLUTZ, Chicago.

FROIN'S SYNDROME. EDUARDO IMBASSAHY, J. de pediat., Rio de Janeiro **3**:289 (July) 1936.

A Negro girl 11 months of age had symptoms of meningitis for fourteen hours. Spinal fluid obtained by puncture revealed no organisms but fulfilled the criteria for Froin's syndrome by being xanthochromic and showing great coagulation. The French literature on this subject is reviewed.

SANFORD, Chicago.

TONSILLOGENIC MENINGITIS: DIAGNOSIS AND THERAPY BY ABSCESS TONSILLECTOMY. J. SCHUBEL, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **139**:389, 1935.

Schubel calls attention to a report by Wessely in which that author described the route by which the pathogenic micro-organisms from a paratonsillar abscess reach the meninges. This report and the realization that the diagnosis of a paratonsillar abscess may be extremely difficult induced him to describe a complicated case that was observed at his clinic: A girl aged 2 had coryza and earache with febrile temperatures. Two weeks later, abdominal pains developed. The practitioner who was consulted at this time and diagnosed the condition as appendicitis and had the child transferred to the surgical clinic. Here the diagnosis could not be corroborated, and the child was sent to the children's clinic, where the abdominal pains disappeared and a catarrhal angina was detected. The tonsils were the size of hazelnuts and met medially. On account of the earaches the tympanic membranes were examined, but they proved to be free from irritation. When after several days the abdominal pains recurred, an appendectomy was performed, but the appendix was free from changes. The postoperative course was uneventful except that the high fever persisted. It was then found that pus escaped from the right ear and that the palatine tonsils were greatly enlarged. An antrotomy was done, but it did not reveal the cause of the suppuration. A radical operation likewise did not clarify the problem. When the bandages were changed, however, pus was seen on the anterior wall of the auditory meatus, and then the perforation of a paratonsillar abscess was thought of. A tonsillectomy was performed, but the puncture of the paratonsillar tissues yielded no pus. An incision on the right side of the neck disclosed only a little pus in the parapharyngeal space, but the abscess membrane and the granulations could be recognized. At that time, however, meningitic symptoms developed, and the child died. In discussing the case Schubel points out that all mistakes could have been avoided if, in view of the high fever, the earaches and the negative results of the otoscopic examination, paratonsillar suppuration had been thought of. He says that he has repeatedly recognized paratonsillar inflammation on the basis of this combination of symptoms. The early removal of the paratonsillar focus of infection would have prevented the endocranial perforation and the fatal outcome.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

THE FUTURE OF CHILDREN WITH CONVULSIONS. EVA BERGEMANN, Monatschr. f. Kinderh. **65**:116 (March) 1936.

Bergemann reviews the case records of one hundred and fifty-five children who were treated for convulsions in the Leipzig children's clinic from 1921 to 1930. Among these, epilepsy played much the most prominent part — fifty-nine cases. The onset of febrile disease was noted in twenty. In a group of twenty-four the condition was classified as on a neuropathic basis, such as pavor nocturnus. Then came the rarer conditions, such as pyknolepsy, spasmus nutans and migraine.

One can never tell whether an epileptic patient will have mental deterioration. Twenty-seven did, and thirty-two did not. One can only surmise such a possibility by noting signs of neuropathic constitution and early changes in character. Petit mal and pyknolepsy offer a better prognosis because the pathologic changes are not so likely to reach the cortex but remain in the basal ganglions. This is probably true for milder epilepsy also. Salaam convulsions and spasms of that sort give a bad prognosis, while the convulsions occurring with the onset of febrile disease and those on the neuropathic basis show tendencies toward spontaneous recovery.

GERSTLEY, Chicago.

A CASE OF MENINGITIS PURULENTA TREATED BY CONTINUOUS SPINAL DRAINAGE. M. MIYAKE and T. HASHIMOTO, Orient. J. Dis. Infants **18**:75 (July) 1935.

A girl 13 years and 5 months old acquired purulent meningitis after an attack of acute otitis media. Bacteriologic study identified the causative organism as a

pneumococcus. A total of 5,348 cc. of spinal fluid was removed by continuous drainage over thirty-seven days. The spinal fluid became normal on the thirty-sixth day after the institution of drainage. The child recovered completely and was able to walk on the fifty-first day after the onset of illness.

KATO, Chicago.

TETANY. J. C. SCHIPPERS, H. J. VAN DER MOLEN and L. VAN DER WILK, Maandschr. v. kindergeneesk **5**:41 (Nov.) 1935.

A case of tetany occurred in a baby of 10 months, who showed during some days symptoms of a lesion of the striatum (athetoid movements and irregular tremor). The possible relation between disease of the parathyroid glands and the cerebrum are discussed. From a group of forty babies treated for tetany from 1921 to 1932 in the "Emma Kinderziekenhuis" twenty-five were reexamined. Only thirteen of these could be considered as normal; of the twelve abnormal children, four were idiots, two epileptic and two weak minded; one had adiposity with infantilism and one diabetes mellitus. This result is in accordance with the observations made by Philippi over the period from 1914 to 1921 in the same hospital. It is impossible to decide in a case of tetany at the onset whether the nervous system is affected or not. However, tetany which shows at the same time distinct signs of rickets may be considered as "benign." The authors finally discuss the value of the symptom of von Pirquet for healing tetany : An O $< 5$. They are of the opinion that this symptom has only a restricted value.

VAN CREVELD, Amsterdam, Netherlands.

## Psychology and Psychiatry

RELATION BETWEEN BINET MENTAL AGE AND MOTOR CHRONAXIA. GEORGE KREEZER and KATHERINE P. BRADWAY, Arch. Neurol. & Psychiat. **34**:1149 (Dec.) 1935.

Chronaxia is a minimum duration of a flow of direct current required to stimulate a tissue with a current of consistent strength. Kreezer and Bradway were interested in determining whether there is a correlation between motor chronaxia and mental age, as determined by intelligence tests. The results were essentially negative.

BEVERLY, Chicago.

CLASSIFICATION OF SCHOOL CHILDREN BY MEANS OF THE HANDWRITING SPEED FACTOR. CLARENCE QUINAN, Arch. Neurol. & Psychiat. **34**:1172 (Dec.) 1935.

Quinan noted an early steplike diminution in writing time from the second grade through high school.

BEVERLY, Chicago.

THE NEXT DECADE AND EDUCATION FROM THE STANDPOINT OF MENTAL HYGIENE. IRA S. WILE, Arch. Pediat. **53**:27 (Jan.) 1936.

This article does not lend itself to abstracting.

WADDELL, University, Va.

STUPIDITY AS EXEMPTION. IDA LOWY, Internat. J. Individ. Psychol. **1**:102 (April) 1935.

When for any reason the adult members of a family assume that a normal child is stupid, the child is likely to accept their evaluation of his intelligence. This springs in part from the intensification of a feeling of inferiority and in part from an actual desire to escape the responsibilities which belong to the normal child. Lowy cites two cases, those of a boy aged 14 and a girl aged 11. In each case the child had been repeatedly accused of being stupid and was accordingly shy and unaggressive. The boy lived in active fear of various "bogies," isolated and lonesome. The girl remained timidly in the background of school or home.

apparently miserably content to accept her inferior status. In each case it was possible to rehabilitate the patient's personality, so that a normal child resulted. The technic consisted of setting before the child tasks easy enough for ready accomplishment, of praising each success, of assuming that the child was normal and of gradually increasing the complexity and difficulty of the task until the child found itself solving difficult problems.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.]

MUSICAL TALENTS OF INDIAN AND JAPANESE CHILDREN. VERNE R. ROSS, J. Juvenile Research **20**:95 (July) 1936.

Musical talents are divided into capacities for the judgment of pitch, intensity, time, consonance, memory and rhythm. Indian children of the sixth, eighth, ninth, eleventh and twelfth grades were tested and their abilities tabulated. They were found to be inferior to white children of the same grades in all these particulars with the single exception that those in the ninth grade were superior in their appreciation of the time component. Similar tests and tables show Japanese children to be the equals of white children.

HAMILL, Chicago.

ON EVALUATING THE RELATIVE IMPORTANCE OR "SERIOUSNESS" OF VARIOUS BEHAVIOR PROBLEMS IN CHILDREN. LUTON ACKERSON, J. Juvenile Research **20**:114 (July) 1936.

From case records on 5,000 children examined consecutively, traits of undesirable behavior were correlated. "Three criteria of seriousness were employed": the personality total, the conduct total and arrest by the police. Thirty-eight larger correlations with the personality total, running from dementia praecox, queerness and depression to unhappy manner, headaches and disobedience, are tabulated: forty-two with the conduct total, from bad language, disturbing influence at home, and psychopathic personality to overinterest in sex matters, robbin and overinterest in the opposite sex; and forty-four with arrest by the police, from truancy, stealing and bad companions to emotional instability, irregular attendance at school and sex delinquency. This is a preliminary report.

HAMILL, Chicago.

UNADJUSTED YOUTH. VIERLING KERSEY, J. Juvenile Research **20**:125 (July) 1936.

Vierling Kersey discusses the problems of the education of children, the increase of education, the inadequacy of opportunity after graduation and the development of interest in security, health and recreation. He points out three needs: a plan, a constructive expression of the energies and a sense of responsibility.

HAMILL, Chicago.

WHERE PRISONERS COME FROM. SANFORD BATES, J. Juvenile Research **20**:130 (July) 1936.

Prisoners, Bates holds, are the product of inadequacy of social surroundings and lack of supervision of leisure time activity. He cites twenty traits of bad boys.

HAMILL, Chicago.

A MENTAL HYGIENE CLINIC IN A HIGH SCHOOL. AN EVALUATION OF PROBLEMS, METHODS AND RESULTS IN THE CASES OF 328 STUDENTS. MARIAN MCBEE, Ment. Hyg. **19**:238 (April) 1935.

After a study of the case records in a mental hygiene clinic associated with a good high school in a middle class neighborhood, McBee classifies behavior problems of adolescence into four groups: those associated with scholarship, truancy and personality, respectively, and a miscellaneous group. The last group included some instances of delinquency and some of conduct disorders based on physical disabilities.

Among the children of foreign-born parents, a disproportionate number of personality problems was found, owing in part to the clash between the foreign culture of the parent and the Americanized standards of the children. This clash tends to produce either shyness or overaggressiveness. Further studies showed that more careful placement of pupils and more experience with self-reliance are needed in the elementary schools of the community. Many difficulties arising from high school scholarships were found to be based on social or personality problems. The need for studying the student as a psychic unit, rather than by fragments, is stressed. Emphasis is also laid on the importance of adequate vocational guidance. The best time for the interview of the student by the social-psychiatric worker was found to be during the second year of high school, and the establishment of this procedure as a permanent routine is urged. The increasing use of the school clinic as a community mental hygiene center is suggested.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.]

THE SUMMER CAMP AS A BEHAVIOR CLINIC. R. L. AMSDEN, Ment. Hyg. **20**:262 (April) 1936.

Camp Onawama, Long Lake, Fenton, Mich., although superficially like other camps, is a behavior clinic conducting experiments in leadership and control, procedures in the adjustment of behavior and direct approach in the rebuilding of attitudes and personality. In reconstructing the behavior of socially maladjusted boys, delinquent and potentially psychotic, the aim is to interpret behavior rather than to judge it, in order to find a socially acceptable way of providing for each child his unsatisfied "wants."

Each boy presents a separate problem, but usual procedures include working out a tentative plan for every camper, establishing his confidence and talking over difficulties to help the boy see facts in their relative values. Direct counseling, indirect treatment, as exemplified in the development of a sense of responsibility through opportunities for leadership, giving of awards and punishments and the use of group approval as a means of social control are usually effective means of forming desirable habits. A large group of boys who had been delinquents before attending Camp Onawama had satisfactory school records the following year. A large proportion of the boys at the camp were no longer problem children when placed in a wholesome environment.

The unusually receptive and cooperative attitude of boys while at camp and their opportunities for intimate association with counselors and directors having fine personalities combine to make a summer camp a desirable locus for a behavior clinic.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.]

FUNCTIONS OF PSYCHIATRY IN A TRAINING SCHOOL FOR JUVENILE DELINQUENTS. CLARENCE O. CHENEY, Psychiatric Quart. **8**:439 (July) 1934.

Many of the factors which precipitate personality disorders are also operative in the bringing about of crime and delinquency. The administration of institutions for delinquents and criminals should be in the hands of persons with psychiatric training or in the hands of officials sympathetic to and cooperative with a psychiatric point of view. It is demoralizing to have recommendations of a psychiatric nature blocked or nullified by lay administrators.

In the institution for delinquents, the psychiatrist should examine each newly admitted child and thereby lay the groundwork for a rapport useful in subsequent psychotherapy. The social service department, so valuable an aid in collecting and interpreting the data from which the psychiatrist will have to draw, should be directly under the psychiatrist's supervision. The industrial officers, cottage masters, school teachers and administrative officials should consult with the psychiatrist on the placement, classification and assignment of each inmate. The selection of the personnel of the cottages when changes are made should be made with the assistance of the psychiatrist. Problems among the officials and within

the official family of the institution should be referred to him. The psychiatrist should have much to say in the disciplining of inmates who are not adjusting themselves properly to the institutional regimen. The psychiatrist should be available for individual psychotherapy whenever requests are made for it by an inmate or by an officer. Finally, the advice of the psychiatrist should play a part in the determination of the time of parole and in the supervision of the paroled inmates.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.]

CONSANGUINITY AND MENTAL DISEASE. MAURICE DESRUELLES and PIERRE GARDIEN, Ann. méd.-psychol. **93**:168 (July) 1935.

When mental disease occurs in a patient born of a consanguineous union, there is a tendency to consider the blood relationship as a predisposing factor. It is based mainly on an old lay prejudice, springing from an ethnic taboo, rather than on scientific observations. The matter has been the subect of lively debate in France since 1913. To arrive at a rationally established conclusion, it would be necessary to examine the ratio of consanguineous to nonconsanguineous or crossed marriages among the parents of persons suffering from mental disease. Since this would be complicated by syphilis and alcoholism, such a study would be almost impossible as a means of determining the issue at question. Moreover, it has been shown by August Voisin in a study of a limited area (the island of Batz) where consanguineous marriages are numerous that the descendants are normal if the parents have been sane and if the ascendants have been normal for several generations. Thus, Voisin claimed that consanguinity per se is not an unfavorable influence on mental health.

Opinion has varied from the middle of the nineteenth century to the present and is divided rather sharply into three periods: 1. Before 1859 a unanimous opinion prevailed. Esquirol, Ellis, Prosper, Lucas and most of their contemporaries were of the opinion that consanguinity of parents, ipso facto, was responsible for mentally defective or prepsychotic children. The conception was accepted in religious, legal, literary and medical circles. Scientists were inescapably influenced by the weight of popular prevailing ideas. No writers denied the morbid influence of consanguinity, but Pinel and a few others did not include it in the etiology of mental disease. 2. From 1859 to 1900 ardent controversy reigned. Notably, August Voisin, Bertillon, Charcot and George Darwin asserted that the offspring of sane consanguines could be normal; Binet and others favored the opposite view, while Falret, Ribot and Kraepelin withheld opinion. At the beginning of this period the partisan groups were of equal size, but toward the end of the century the innocuity of consanguinity rose in favor. 3. Since 1900 writers on the subject have been almost unanimous in supporting the innocuity of consanguineous marriages of sane parents.

The importance of distinguishing sane from morbid heredity is obvious.

MOORE, Boston. [ARCH. NEUROL. & PSYCHIAT.]

A PHYSIOLOGIC STUDY OF A MENTALLY DEFICIENT CALENDAR CALCULATOR. GONZALO R. LAFORA, Encéphale **30**:309, 1935.

The lack of cooperation of the mentally deficient person makes it difficult to obtain information about the mechanism of such abilities as rapid calculation and memory for dates, names or unrelated events. Witzel reported the case of an imbecile, aged 22, who reduced all arithmetical operations to multiplications of 16 which she had memorized by placing buttons in groups of 16. Thus, she had found that $23^2 = 33 \times 16 + 1$ and $36^2 = 81 \times 16$. The aptitude for calculating dates was studied by Blin in an oligophrenic boy, aged 12 years, who could not do simple arithmetic but could tell without hesitation the day of the week of any date within the three years preceding and the year following the current one. When asked how he did this, he replied only: "Because I know." Following a suggestion of Binet, Piéron in this case found the reaction time shorter for dates close to the current time than for those more distant. He concluded that for the former

simple memory was used and for the latter some simple operation. Dupain pointed out the existence of formulas used by professional calculators which could serve for a period of twenty years. But it was incredible that this young moron should know, let alone employ, such methods.

Lafora's case resembles the former. Its special interest lies in the aptitude and willingness of the subject to explain her modus operandi. The patient, a girl aged 15, became mentally retarded and epileptic after typhoid at 4 years. Her intelligence quotient was 65. In spite of schooling and a great desire for education, she could learn only by rote. She possessed a great mechanical memory for past events, dates, rules of grammar and multiplication tables but could not do simple arithmetic without a great many errors and was unable to solve such problems as the change-making tests of the Binet scale even when she could do the corresponding subtraction. She could calculate in from two to eight seconds the day of the week corresponding to any given date, or vice versa, within the three years preceding or the two years following the current year. Her reaction time was notably less than that of a professional calculator which the author had the opportunity of studying. "The essence of her procedure consists in her reliance, for each reply, on two or three coinciding data which are supplied by her mechanical memory. Through frequent repetition the mnemonic act is almost automatic and the data reach her imagination with great precision. These data are supported by rules of relation and coincidence which she has noted by the comparative study of the calendar for several years—her favorite pastime since the age of 9." These are what Müller called the natural aids to memory. Thus, to choose from numerous examples given, she knows that January 7 of nonleap years corresponds to the same day of the week as October 1; that January 1 of any given year corresponds to a day of the week following that of the preceding year, save for leap years, which advance two days; that the months of 1931 were identical with those of 1925. Very little actual arithmetic is involved in such operations.

For comparison, the mechanisms employed by intelligent "memory artists" are described. The famous little shepherd, Henri Mondeux, studied by the Paris Academy of Sciences in the early nineteenth century, knew by heart the squares of all numbers up to 100. He had further discovered independently a number of rules such as Newton's binomial theorem. To find the square 2,435, he separated that number into two lesser ones, 24 (00) and 35. $2{,}435^2 = 24^2 + 2 \times 24 \times 35, + 35^2$ with the proper zeros added. As the values of $24^2$, $24 \times 35$ and $35^2$ were known by heart, the operation was reduced to a simple addition. Among the other examples given are the case of Caneljas, who could commit to memory rapidly enormous series of unrelated data; of Jaurès, who after a single reading could deliver one of his speeches translated into a language of which he was ignorant. The most extraordinary calculator was Dr. G. Rückle, himself a noted mathematician, studied by Müller and Kroh. Rückle could repeat a series of forty-eight numbers after a learning period of 44 seconds or seventy-two numbers backward after one hundred and thirty-seven seconds. He used such mnemotechnic devices as the facts that the side of a circumscribed dodecahedron is 0.535, that the first year of the reign of Cyrus was 559 or that the log of 13 is 1.86, all of which he knew by heart and employed to establish associations with otherwise unrelated numbers. All these methods are fundamentally of the same order as that used by the mentally deficient calendar calculators, but on a different scale.

LIBER, New York. [ARCH. NEUROL. & PSYCHIAT.]

TEST OF PRACTICAL INTELLIGENCE IN CHILDREN. M. LAMBERCIER and A. REY, Arch. de psychol. **25**:1, 1935.

The behavior of children in a practical situation is studied through their attempts to secure a piece of candy fixed to one end of an iron rod suspended out of reach and procurable only through a roundabout method. Toward the middle of the rod is a U-shaped bend. As the rod hangs horizontally this bend is within the child's reach. By pulling on this and manipulating the rod properly he can secure the candy. The group used for the main test consisted of about eighty

children aged from 4 to 8 years, otherwise not described by the authors. The responses made by these children are differentiated into various groups, the most important of which are: (1) attempts to reach the candy directly, a method persisted in by about a fourth of the children and adopted at first but given up readily by another fourth and (2) attacks on the U-shaped bend, a method characteristic of another fourth of the children and, in general, more characteristic of the older children. Lambercier and Rey discuss in detail the evolution of practical intelligence, as it is shown by this test, from a neuromuscular level to the higher level at which the motor possibilities of the body are realized, the direct route to the goal is inhibited and a roundabout route is substituted.

McBride, Philadelphia. [Arch. Neurol. & Psychiat.]

Mental Defect of the First Born. Hans Luxenburger, Monatschr. f. Kinderh. **65**:109 (March) 1936.

Luxenburger criticizes a former article in which E. Kleindienst states that the percentage of cases of subnormal mentality is higher in the first born. He submits tables and gives mathematical analysis to show that such a conclusion is probably not well founded. He also takes exception to the idea that the defect is due to birth injury and expresses the belief that in about 80 per cent of cases the condition is on a hereditary basis.

Gerstley, Chicago.

Schizophrenia in Early Childhood. E. Grebelskaja-Albatz, Schweiz. Arch. f. Neurol. u. Psychiat. **34**:244, 1934; **35**:30, 1935.

In twenty-two cases of schizophrenia studied, the patients' ages ranged from 3½ to 8 years, and the period of obstruction, from six months to three and one half years. A brief history is given in each of the nine cases with an acute onset. Hereditary taint was generally lacking in this group, and the children seemed to have been normal prior to the appearance of the psychosis. With one exception, the ages of the children at the onset of the disease fell between 2½ and 3 years in all nine cases. Anxiety states, motor unrest, disturbed sleep and dulling of affect with loss of former disorders were frequent early symptoms. Negativism, stereotyped actions and other manifestations of catatonia were observed. Two of the children had definite hallucinations, and the behavior of two others indicated that they were hearing voices. The further course was characterized by deterioration of the personality with intellectual defect of varying degree. In the author's words: "The further development of these children is extremely unproductive."

In the remaining thirteen cases it was impossible, with one exception, to determine the age of the patient at the onset of the psychosis. Anomalies of development were noted in nine instances, and, in contrast to the first group, schizophrenia was of frequent occurrence in the antecedents. Disturbances in thinking, ambivalence, apathy, dulling of affect and other emotional peculiarities were characteristic symptoms. The normal interests of childhood were generally lacking. The children were in much poorer physical condition than were those in the first group; stigmas of degeneration and vasomotor changes were common. The course, in general, was slowly progressive, with intellectual impairment, difficulties of adjustment and change in personality, although deterioration was less marked in this group.

Daniels, Denver. [Arch. Neurol. & Psychiat.]

## Diseases of the Genito-Urinary Tract

Enuresis in Children. J. V. Bickford, Virginia M. Monthly **63**:271 (Aug.) 1936.

The term "enuresis" is used to cover cases in which after a very complete physical examination no evidence of organic lesion can be discovered to account for the complaint. Bickford regards enuresis as a disorder of conduct, and in

the series of twenty-six cases reported it was associated with one of the following difficulties of personality—unsatisfactory feeding, temper tantrums, nail biting, hypochondriasis, masturbation, fear reactions, encopresis. There was observed in the majority of cases a general immaturity and failure to accept responsibilities in keeping with the age. Enuresis should be regarded as a symptom and treatment directed toward the child as a psychobiologic unit. The therapy includes: (1) convincing the child and the parent of their ability to overcome the difficulty and obtaining their cooperation; (2) explaining in simple terms methods of assistance, such as limiting fluids; (3) adjusting the environment to remove any stress and strain that lead to psychic disturbance. By the procedures named cure or improvement was obtained in 84 per cent of the cases reported.

STONE, Richmond, Va.

SPECIMEN: POLYCYSTIC KIDNEYS FROM A CASE OF RENAL RICKETS. WILFRID SHELDON, Proc. Roy. Soc. Med. **28**:1074 (June) 1935.

A patient was first seen in 1927, at the age of 4 years, when a hard irregular lump was felt in each loin at the site of the kidneys. The urea concentration test showed very poor kidney function. In 1932 he was admitted to the hospital suffering from thirst and polyuria, and at this time he was noticed to be knock-kneed. Roentgenograms of the long bones showed typical rickety changes. In 1935 he was readmitted to the hospital for the purpose of having a plaster on the legs, but shortly after admission he began to show clinical signs of uremia, which in a few days resulted in his death at the age of 12 years.

Reports of the postmortem examination of the urinary tract and of the long bones are enumerated.

WILLIAMSON, New Orleans.

RELATIONSHIP BETWEEN EXTRAGENITAL TUBERCULOSIS AND THE AGE AT THE FIRST MENSTRUATION. P. NOBÉCOURT, S. B. BRISKAS and A. ABAZA, Progrès méd., July 18, 1936, p. 1185.

No significant variation from normal in respect to age at the first menstruation was discovered in a study of 105 tuberculous girls from 10 to 17 years of age.

LESLIE, Evanston, Ill.

## Diseases of the Ductless Glands; Endocrinology

DIABETES TODAY AND TOMORROW. E. P. JOSLIN, Ann. Int. Med. **10**:179 (Aug.) 1936.

The importance of protamine insulin in the treatment of diabetes mellitus is stressed and its advantages over those of old insulin are numerated.

The etiologic importance of heredity in diabetes is discussed and its importance defined.

Exercise, camps and boarding schools for diabetic patients and wandering nurses for diabetic patients are mentioned in their relationship to the effective treatment of the disease. In addition, hospital training for those suffering with diabetes is urged, and a plea is made for closer supervision and more efficient follow-up methods in dealing with them.

READING, Galveston, Texas.

MIGRAINE: A CRITIQUE OF THE HYPOPHYSEAL THEORY. WALTER TIMME, Bull. Neurol. Inst. New York **5**:437 (Aug.) 1936.

Timme feels that the symptoms of migraine are due to swelling of the pituitary gland in a certain type of person. He feels that the pain is produced by the stretching of the diaphragm of the sella. The other symptoms are produced by the physical forces applied on the surrounding structures and by the increased and changed activity of the gland.

BEVERLY, Chicago.

THYROID "POISONING" IN CHILDREN. HERMAN M. JAHR, Nebraska M. J. **21**: 388 (Oct.) 1936.

Three cases are reported in which large doses of thyroid extract were taken. In the first case, a child 3 years of age swallowed eighteen pills containing 2 grains (0.12 Gm.) each. There were no toxic symptoms. In the second case, a child 20 months of age ate between 40 and 43 grains (2.56 and 2.75 Gm.) of thyroid extract. The following day there were several loose stools. There were no other symptoms or signs of poisoning. In the third case, a 3 year old boy swallowed between 40 and 44 grains (2.56 and 2.81 Gm.) of thyroid extract. There were no symptoms of poisoning. Apparently the product was fresh and from a reputable house in each case. HAMILTON, Omaha.

THE DIABETIC CHILD. L. R. RIELY, Texas State J. Med. **30**:369 (Oct.) 1934.

Riely gives a rather comprehensive review of diabetes as a disease of metabolism and particularly as it is found in the child. Some of the high lights are as follows:

Diabetes is now more common than is generally supposed. Many cases are overlooked because the condition is commonly believed to be a disease of late adult life, rarely occurring in infancy and childhood. The number of cases with onset in childhood parallels the number with onset in old age.

The age of greatest incidence is the same as the period of greatest growth, i. e., from 6 to 8 and from 12 to 14 years. The tall child and the obese adult are susceptible to diabetes.

The reason the diabetic child is stressed is that since the discovery of insulin a practical method of handling the young patient has been available. The well treated diabetic child grows as fast and matures as normally as siblings, collaterals, friends or relatives who are not so handicapped.

Diabetes in childhood has a different underlying pathologic disturbance of the pancreas than that in the older patients.

The rôle of heredity in the development of the diabetic patient is discussed, also the influence of infection, exercise and coma. KNICKERBOCKER, Dallas, Texas.

A CASE OF THYROID INFANTILISM. ROUDINESCO and NICOLAS, Bull. Soc. de pédiat. de Paris **32**:706 (Dec.) 1934.

A boy, 14½ years old, measured 1 meter and 25 cm. tall, was somewhat obese, had thickish skin and considerable delay of ossification and showed some delay in the development of puberty. Despite negative results obtained by interferometric and metabolic tests, thyroid extract was administered. It is considered that this therapy confirmed the belief that the thyroid gland was at fault, because the boy improved and grew 10 cm. in nine months. BENJAMIN, Montreal, Canada.

CONGENITAL INFANTILE MYXEDEMA. B. DANES, Paidoterapia **14**:941 (Feb.) 1936.

Danes reports congenital infantile myxedema in a boy of 4 and a girl of 3 who present every likeness to the true cretin. He discusses the diagnosis and treatment.

HERRON, Spokane, Wash.

CLINICAL STUDIES ON THE INFLUENCE OF EPINEPHRINE, POSTERIOR PITUITARY AND RACEMIC EPHEDRINE ON THE RESORPTION OF INSULIN. VILHELM CLAUSEN, Bibliot. f. læger **128**:64 (March) 1936.

Clausen gives a detailed review of experiments illustrating the effect of epinephrine, posterior pituitary and racemic ephedrine on the resorption of insulin. The latter accelerates the resorption, while epinephrine and posterior pituitary inhibit it. The lowest concentration of epinephrine with distinct effect was found to be 1:200,000. The addition of epinephrine to the insulin gives a delay in the absorption of the latter so that the concentration of the blood sugar falls more slowly than after the administration of insulin alone. Patients with diabetes in whom the fasting blood sugar is not particularly high show a more favorable

course of the blood sugar curve when epinephrine is added to the insulin than with insulin alone, whereas patients in whom the fasting blood sugar is high often show a more unfavorable course of the whole blood sugar curve when the effect of insulin is delayed by the addition of epinephrine than when insulin is given alone. The effect of epinephrine on the blood sugar curve is present only when it is mixed with the insulin and is not due to a general action of the epinephrine. The amounts of epinephrine added to the insulin are perfectly harmless as far as the general action of epinephrine is concerned. There were no subjective complaints or objective signs at the site of injection. The insulin in the epinephrine-insulin mixtures does not lose any of its specific qualities.

WALLGREN, Gothenburg, Sweden.

## Diseases of the Muscles, Bones, Joints and Lymph Glands

OSTEOMYELITIS OF INFANTS. WILLIAM T. GREEN and JAMES G. SHANNON, Arch. Surg. **32**:463 (March) 1936.

On the basis of a study of ninety-five cases of osteomyelitis in children, Green and Shannon conclude that osteomyelitis of infants differs greatly from that of older children not only in many clinical features but also in many principles of therapy. Osteomyelitis in infants under 2 years of age is not rare. Antecedent extra-osseous infection occurred in 55 per cent of the children. These infections usually occurred either in the respiratory tract or on the skin. A definite history of trauma was not often obtained. Bacteriologic studies showed that Staphylococcus aureus was the offending organism in 91 per cent of the older children (from 2 to 12 years) while in the group of infants Streptococcus haemolyticus was by far the predominant organism. Staphylococcic osteomyelitis definitely caused a higher mortality rate than streptococcic osteomyelitis in infants under 2 years.

The early clinical picture of acute osteomyelitis in infants is not essentially different from that seen in older children—acute illness, with the general systemic manifestations provoked by sepsis, together with local pain and sensitivity of the involved part. The severity of the onset and subsequent illness is as variable in this group as in older children. The differential diagnosis demands the particular consideration of sepsis of the joints, infection of the soft tissues and scurvy with infection elsewhere.

The treatment was surgical except in the cases in which the patient was moribund. An operation on the bone was performed, usually the formation of a window. If the infant survives the acute infection, the prognosis for sound bones is excellent. Recurrence almost never occurs. Great care is given to the surgical treatment in order to prevent sequestration. If the condition of the infant is such that operation seems unwise, supportive treatment should be given and operation performed later. The sound advice given by the authors offers a valuable guide in the handling of infants with this disease.

CONVOLUTIONAL DIGITATIONS SEEN IN ROENTGENOGRAMS OF IMMATURE HUMAN SKULLS. L. M. DAVIDOFF, Bull. Neurol. Inst. New York **5**:61 (Aug.) 1936.

Convolutional markings in roentgenograms of the skulls of children, though sometimes present to a marked degree, are without pathologic significance. Davidoff studied these markings in about 2,500 normal persons. No markings occurred before 9 and very few before 18 months of age. From this point the digital markings increased rapidly to the age of 4 years, then continued at a level to the age of from 7 to 9 years, and thereafter fell off rapidly, reaching the lowest point at the age of 14 years. The curves of individual bones have the same general form and show variations at given times.

BEVERLY, Chicago.

PAGET'S DISEASE: RELATIVE CONSTANCY OF SERUM PHOSPHATASE LEVELS OVER PERIODS UP TO TWO YEARS. A. B. GUTMAN and E. B. GUTMAN, Proc. Soc. Exper. Biol. & Med. **33**:150 (Oct.) 1935.

In a great majority of cases of Paget's disease, the phosphatase values remain high for a long period. This finding should be useful in supplementing the clinical and roentgenographic examinations.

HANSEN, Minneapolis.

STAPHYLOCOCCAL ANTIHEMOLYSIN-TITERS FOLLOWING STAPHYLOCOCCAL TOXOID IN CHRONIC OSTEOMYELITIS. J. E. BLAIR and F. A. HALLMAN, Proc. Soc. Exper. Biol. & Med. **34**:637 (June) 1936.

Thirty-eight patients with chronic osteomyelitis were given therapeutic injections of staphylococcic toxoid. A definite rise occurred in the antihemolytic titer of the serum in all thirty-eight cases. No corresponding improvement in the clinical condition occurred.

HANSEN, Minneapolis.

SYNDROME OF BLUE SCLERA. P. BONNET and P. WERTHEIMER, Ann. d'ocul. **172**:226 (March) 1935.

Bonnet and Wertheimer report the case of a patient affected with blue sclera, which is characterized by: (*a*) fragility of the bones; (*b*) a blue color of the scleras and (*c*) deafness, as reported by van der Hoeve. The family history of the patient confirmed the hereditary nature of the disease.

BERENS, New York. [ARCH. NEUROL. & PSYCHIAT.]

PRIMARY MYCOSES OF THE BONE. E. ALLENBACH and M. ZIMMER, Rev. franç. de pédiat. **11**:168, 1935.

Mycoses of the bone occur most frequently in the calcaneus. Three cases are reported, in all of which there was a marked degree of sclerosis as determined by roentgenograms. In two the sulfur granules of actinomycosis were obtained, and in the third the condition was a blastomycosis. In all the disease cleared up after surgical treatment and large doses of iodides.

LESLIE, Evanston, Ill.

CHONDROMA OF THE SPINOUS APOPHYSIS OF THE FIRST LUMBAR VERTEBRA SIMULATING POTT'S DISEASE. PEYCELON and AUFRÈRE, Rev. d'orthop. **23**: 152 (March-April) 1936.

A boy of 12 years complianed for six months of pain and soreness over the dorsolumbar region. The parents noted a small swelling near the spine, low on the back. Roentgenograms were negative, but since the clinical signs were suggestive of Pott's disease, immobilization was carried out. No further symptoms developed; the pain and soreness disappeared, and the general health improved. The parents noticed, however, that the swelling was increasing. The authors examined the boy at that time, finding a firm mass the size of a nut and slightly tender lying over the first lumbar vertebra. Movements of the spine were somewhat limited by muscular contraction. No neurologic signs were present. Roentgenograms at that time revealed an osteocartilaginous tumor located at the end of the spinous process of the first lumbar vertebra. At operation a tumor was found attached by a pedicle to the spinous apophysis. The apophysis was sectioned, and the tumor was removed in toto. Healing occurred without incident. Histologically the tumor was an enchondroma.

RYAN, Vancouver, Canada.

PROGRESSIVE MYASTHENIA WITH PARTICIPATION OF THE SMOOTH MUSCLES OF THE EYE. V. RABINOVITCH and G. VENGRJENOVSKY, Rev. d'oto-neuro-opht. **12**:758 (Dec.) 1934.

Progressive myasthenia has been considered a primitive disease of striated muscles, although isolated cases have been observed in which the manifestations

have extended to the smooth muscles of the urinary bladder and to the intrinsic muscles of the eye. In the case reported, the patient, a laborer aged 22, complained of visual disturbances, diplopia and ptosis of the right eye. The trouble began at the age of 12, following a violent fright, and had progressed slowly. Examination revealed pupils that were equal but continually varied in size, with narrow palpebral slits and ptosis. While the patient was fixing on an object, diplopia appeared after ninety seconds and was relieved by closing the eyes. Consecutive tests showed a progressively shorter interval of freedom from diplopia after fixation. When the patient followed the finger with the eyes for ninety seconds, convergent strabismus appeared, but it was quickly relieved by rest. Convergence was intact at first, but marked insufficiency of the internal rectus muscles soon occurred. A similar fatigability was observed when the patient attempted to accommodate: the near point receded rapidly until after four minutes reading was impossible. Visual activity varied from 0.3 to 0.8, and glasses did not improve it. Skiascopic examination revealed bilateral myopia, varying from 1 to 3 and 4 diopters; after atropinization the myopia was replaced by hyperopia of 1.5 diopters. The orbicular, frontalis and extensor muscles of the neck exhibited marked fatigability. No additional abnormalities were discovered.

Besides essential myasthenia, symptomatic myasthenia may follow typhus, epidemic encephalitis, malaria, diphtheria and tuberculosis. No report of fatigability of the ciliary muscle in myasthenia was discovered in the literature. Fatigability of the ciliary muscle in a myasthenic patient must be considered a myasthenic phenomenon. This view harmonizes with the modern conception of myasthenia: that it is an essential disturbance of the function of the sarcoplasm of striated muscle. This function is identical with the function of smooth muscles; both are characterized by tonic contraction. Participation of the smooth muscles in myasthenia is explained by the neurovegetative theory of this condition. There is certainly a hypofunction of certain sympathetic fibers going to the myasthenic muscles, which is proved by: (1) aggravation of the myasthenic symptoms by the action of ergotamine, which paralyzes sympathetic filaments; (2) extreme fatigibality in Addison's disease, and (3) extreme fatigability in muscles from which the sympathetic nerve supply has been removed. If it is true that myasthenia is caused by disease (infection) of the meso-encephalic and diencephalic neurovegetative centers, with consecutive hypotonia of the sympathetic nerve, the spasm of accommodation may be the effect of secondary vagotonia. Instability of the tonus of the ciliary muscles may explain the variations in refraction observed in the case reported.

DENNIS, Colorado Springs, Colo. [ARCH. NEUROL. & PSYCHIAT.]

MATERNAL BONE GRAFT IN A CASE OF OSTEOPSATHYROSIS. C. KETELBANT, Scalpel **88**:1040 (Aug. 17) 1935.

A child of 4½ years suffered nine successive fractures in the femur, the tibia and the forearm. The Wassermann reaction of both the mother and the child was negative. A diagnosis of osteopsathyrosis was made on the ground of blue sclerotics, repeated fractures from slight trauma, the age of the child, compression of the vertebrae and rarefaction in the thorax. Examination of the blood showed calcium 0.108 and inorganic phosphorus 0.04 Gm. per liter. After the eighth fracture, which occurred at the lower third of the left femur, Ketelbant inserted a graft taken from the mother's tibia. Three months later callus had formed, and the entire femur was calcified.

VINTON, New York.

ABNORMAL BRITTLENESS OF THE BONES IN A FAMILY. H. FUSS, Arch. f. klin. Chir. **182**:425 (July) 1935.

Fuss presents a patient with idiopathic osteopsathyrosis. The mother and a sister had similar conditions. An extensive bibliography is given, with discussion of etiology and diagnosis.

DAFFINEE, Boston.

FENESTRAE PARIETALES SYMMETRICAE. ERICH HASSLER, Monatschr. f. Kinderh. **64**:337, 1936.

Hassler reports a case in which roentgenograms showed congenital defects in the parietal bones of a 3 year old girl. The family history showed frequent premature births and a tendency to congenital abnormalities.

GERSTLEY, Chicago.

LEONTIASIS OSSEA. IRMGARD SCHARFF, Monatschr. f. Kinderh. **65**:100 (March) 1936.

A history, photographs and roentgenograms of an 11 year old girl are given. From the sixth year there had been a gradually enlarging painless swelling of the upper jaw bone, near the root of the nose. At first, histologically, the condition was diagnosed as ostitis fibrosa. Later, however, it was diagnosed as syphilis.

GERSTLEY, Chicago.

TREATMENT OF PROGRESSIVE MUSCULAR DYSTROPHY. München. med. Wchnschr. **83**:1013 (June 19) 1936.

The author of this article prefers to remain incognito. He has had progressive muscular dystrophy for thirty years. In a most interesting report he records his observations on himself when taking amino-acetic acid. He was almost completely incapacitated, but since taking this drug he has regained enough strength to be able to practice eight hours a day. However, he believes the condition continues to progress, though slowly.

For more than a year he took 15 Gm. of amino-acetic acid daily. Then he began to lose muscle strength, experienced fatigue and required excessive sleep. These symptoms disappeared when the drug was discontinued for ten days. For the next six weeks the drug was not taken. After that period there was loss of muscle strength, and the drug was taken again, starting with small doses.

Amino-acetic acid in overdosage produced an interesting condition. The author noticed in the epidermis crops of submiliary pustules which gave the impression of septic emboli. These blebs increased in size and formed painful furuncle-like lesions. The eruption lasted several weeks and showed a tendency to heal only after amino-acetic acid was not taken for a few days. Subsequently the eruption was avoided by stopping the drug as soon as there was pruritis or the appearance of pinhead-sized areas of redness in the skin.

The following schedule for taking amino-acetic acid was found the best: 5 Gm. daily for ten days and then two days' rest; after six weeks a rest of six days. A longer rest resulted in loss of muscle strength. The author agrees with the observation of others that when the muscles are used to excess the amount of amino-acetic acid required is greater. Under such circumstances the daily dose is increased to from 10 to 15 Gm.

A diet with plenty of sugar is necessary. The author does careful exercises to maintain the strength of his muscles. He finds that a proper mental attitude is necessary for improvement. Self-pity and resignation are deplored.

BRAHDY, Mount Vernon, N. Y.

LYMPHADENOSIS OF THE BONE MARROW. A. F. ZANATY, Virchows Arch. f. path. Anat. **294**:80, 1934.

To a previously reported case of what Zanaty terms primary medullary lymphadenosis (abstr., *Arch. Path.* **19**:885 [June] 1935), he adds two cases, both in girls aged 4 years. In these, as in the previous case, the condition ran an aleukemic course, and the predominating clinical feature was anemia. He believes that it is necessary to recognize as a special form of lymphadenosis or leukemia a form characterized clinically by early anemia. In this respect it is like myeloid leukemia, in which anemia is an early manifestation, in contrast to the usual form of lymphoid leukemia, in which anemia is a relatively late manifestation. Anatom-

ically the condition under consideration is characterized by replacement of the bone marrow by proliferating lymphoid tissue. He derives the hyperplastic tissue from indifferent mesenchymal stem cells of the marrow, with differentiation of the tissue into lymphocytes. He accepts the unitarian doctrine of the origin of both myeloid and lymphoid cells in the bone marrow, at least under pathologic conditions, from an indifferent stem cell.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

A CASE OF SO-CALLED KÖHLER'S DISEASE. K. TOKI, J. Orient. Med. **24**:90 (June) 1936.

Köhler's disease of the right navicular bone was diagnosed in a boy 8 years old by an x-ray picture. He had had an injury about three months previously, resulting in some swelling which did not last long. He continued, however, to have a slight limp. The x-ray picture showed the right navicular bone to be streaked with rather thick shadowy lines, leading one to think that there had been a compression fracture in which the parts had been pressed together.

LESLIE, Evanston, Ill.

## Diseases of the Eye

PULSATION OF THE EYEBALL ASSOCIATED WITH DEFECTS IN THE WALL OF THE ORBIT. J. M. WHEELER, Bull. Neurol. Inst. New York **5**:476 (Aug.) 1936.

Pulsation of the eyeball may be due to a communication between the cranial and the orbital cavity. Usually a large part of the roof of the orbit is absent. Such a defect may be due to a congenital anomaly or to a plexiform neurofibromatosis of the orbit (Recklinghausen's disease).

Pulsation of the orbit in the presence of a large aperture in the roof is synchronous with pulsation of the radial artery. The impulse is transmitted from the brain and does not produce subjective symptoms as does that accompanying an arteriovenous communication. Pulsation of the eyeball may occur early in Recklinghausen's disease but may disappear later. BEVERLY, Chicago.

COD LIVER OIL AS LOCAL TREATMENT FOR EXTERNAL AFFECTIONS OF THE EYES. E. STEVENSON, Brit. J. Ophth. **20**:416 (July) 1936.

In support of his conclusions, the chief of which is that cod liver oil has undoubted and rather surprising efficacy as a healing agent, Stevenson cites several conditions, including burns of the lids, eyeball and cornea, dendritic ulcer and relapsing keratitis, in which this agent was used with success. The notes on 150 patients treated at the clinic indicate that use of cod liver oil has greatly reduced the "pre-oil" number of necessary attendances. Its use should be withheld in the early stages of hypopyon keratitis. Cod liver oil applied locally seems to promote the growth of natural tissues and to inhibit that of scar tissue in any case in which there is loss of substance. ZENTMAYER, Philadelphia. [ARCH OPHTH.]

A CASE OF EXUDATIVE RETINITIS WITH ANGIOMAS (COATS' DISEASE) IN A CHILD OF FIVE YEARS. M. A. DOLLFUS, Bull. Soc. d'opht. de Paris, April 1936, p. 308.

The patient had sudden loss of vision in the left eye. The eye had been divergent for the past two years. The right eye was normal, with 10/10 vision. The pupil of the left eye was in semimydriasis, regular but nonreactive to direct light, and the vision was gone. The coexistence of exudative retinitis, detachment of the retina, deposits of cholesterol and small miliary aneurysms corresponds exactly to Coats' description. Dollfus asks advice as to the treatment of the condition. A drawing of the fundus is included. MAYER, Chicago. [ARCH. OPHTH.]

THE EARLY DETECTION OF DALTONIAN PATIENTS IN SCHOOLS. V. KOVARSKY, Rev. méd.-sociale de l'enf. **4**:166 (May-June) 1936.

Kovarsky divides daltonism (color blindness) into (1) absolute, in which the subject cannot distinguish red from green or (more rarely) blue from yellow, (2) relative, in which the patient can with difficulty distinguish red from green or blue from yellow, and (3) total, in which there is no vision for color.

In examining 135 boys from 11 to 12 years of age with charts supplied by Professors Pech and Villard and Dr. Viallefort of the University of Montpellier, he found 37 per cent daltonians (17 per cent absolute and 20 per cent relative) and 40.7 per cent who had some slight difficulty in distinguishing colors. He found also 4.4 per cent totally color blind.

He thinks that the reason his figures are so high in comparison with others is that his subjects were younger and had not yet learned of their disability and of how to conceal it. He thinks such tests should be made in all elementary schools in order to keep color-blind subjects out of professions unfitted to them.

BROWNE, Detroit.

## Skin Diseases; Allergy

DESENSITIZATION OF SKIN SITES PASSIVELY SENSITIZED WITH SERUM OF PATIENTS WITH HAY FEVER; CROSSED REACTIONS OF DIFFERENT POLLENS; VARIATIONS IN THE RECIPIENT. F. M. RACKEMANN and H. C. WAGNER, J. Allergy **7**:319 (May) 1936.

Fifty-eight patients with negative histories as regards pollens and negative skin tests, from the clinic for allergy, were used in the experiment.

Their skin was passively sensitized with serums known to contain reagins to the antigens that were to be used to desensitize. It was found that treatment of a passively sensitized site with timothy, orchard grass or red top resulted in most instances in simultaneous desensitization to the other two grasses. This was not true of sweet vernal, plantain or ragweed. Birch desensitized to oak, maple and willow in most instances, but none of these desensitized to birch. Variations sometimes occurred, such as a reaction to the primary dose of the sensitizing serum, a flare following the first treatment of the passively sensitized skin, and sensitiveness of the entire skin. Such occurrences may depend on the particular recipient.

HOYER, Cincinnati.

PROTEIN CONTENT OF HUMAN SERUMS: ANALYSES OF SERUMS BEFORE AND AFTER POLLEN INJECTIONS. ARTHUR STULL, MARY GLIDDEN and MARY LOVELESS, J. Allergy **7**:333 (May) 1936.

The problem was to determine whether treatment of pollen-sensitive persons with pollen extract caused any quantitative change in the serum proteins. Serum from nineteen persons who had positive skin reactions were studied before and after treatment. Seventeen of these persons had had no previous treatment; two had been treated the previous season. Serums from normal persons were studied.

The albumin-globulin ratios and pseudoglobulin-protein ratios showed no significant change before and after treatment. They were in close agreement with the ratios obtained from the normal serums. HOYER, Cincinnati.

THE LEUCOPENIC INDEX IN ALLERGIC DISEASES. H. J. RINKEL, J. Allergy **7**:356 (May) 1936.

The article is a report of the leukopenic index in 537 instances in 56 patients suffering from various forms of allergy. Rinkel believes, as does Vaughn, who reported his findings in 1934, that this index has definite value as an aid in diagnosis. He points out its limitations and clinical applications and states that the accuracy of a single count forty minutes after a meal is 80 per cent of that of 3 counts at twenty minute intervals following the meal.

In the discussion Dr. Ralph H. Spangler brought out that in his limited experience the lymphocytes predominate in the leukopenia accompanying clinical symptoms, whereas the polymorphonuclear cells predominate in that in the absence of symptoms.

HOYER, Cincinnati.

## Surgery and Orthopedics

MORTALITY FROM AUTOMOBILE ACCIDENTS AMONG CHILDREN IN DIFFERENT GEOGRAPHIC REGIONS OF THE UNITED STATES. W. M. GAFAFER, Pub. Health Rep. **51**:1083 (Aug. 7) 1936.

Among children under 15 years of age there were 22,044 deaths from all accidents in 1930 and 10,629 deaths from measles, scarlet fever and diphtheria. Mechanical suffocation leads among all accidents at ages under 1 year, burns at 1 to 2 years and automobile accidents at 4 to 15 years. In the order of regions, the accident rate per hundred thousand children under 15 years of age is, northeastern, 17.4; western, 16.1; north central, 14.8, and southeastern, 9.1. However, in calculating deaths per hundred thousand registered automobiles the order is, northeastern, 24.4; southeastern, 22.1; north central, 16.4, and western, 13.5. The last order remains unchanged when deaths per fifty million gallons of consumed gasoline is used as a standard of comparison. SANFORD, Chicago.

SURGICAL OPERATIONS IN EARLY INFANCY. ANDRÉ MARTI, Nourrisson **24**:147 (May) 1936.

Operations for congenital anomalies amenable to surgical treatment are described, e. g., imperforate anus, congenital stenosis of the small intestine, congenital obliteration of the bile ducts, umbilical hernia, defects of the urogenital tract, encephalocele and spina bifida. MCCLELLAND, Cleveland.

ESSENTIAL COXA VARA. M. LEEMANS, Rev. d'orthop. **23**:33 (Jan.-Feb.) 1936.

Leemans reports a case of a child 16 years of age who showed coxa vara in the right hip after an accident. At that time the left hip showed some irregularity in outline, with a slightly prominent and thickened line between the head and the neck of the femur. Ten months later, the left hip showed the typical lesion of coxa vara.

By comparing roentgenograms of the normal hip joint and those of a hip affected by coxa vara certain definite changes can be noted. In the head of the normal femur the greatest part lies behind, the internal extremity is pointed and the point is directed downward, the superior and internal part of the head being most developed. In the heads of femurs predisposed to coxa vara or in which the disease is in its primary stage, the greatest part of the head lies internally and the external tip is most pointed.

The author also points out that in this instance the fossa for the round ligament was well formed, without any evidence of decalcification. This would disprove Huc's hypothesis that coxa vara is the result of impaired blood supply to the head of the femur through the round ligament. As has been stated, the line of union between the head and the neck of the femur was prominent; that is, there was delayed calcification. In the author's opinion coxa vara is the result of minor injury to a hip already the seat of delayed union. RYAN, Vancouver, Canada.

TREATMENT OF CONGENITAL INVERTED CLUBFEET. BARBOZA VIANNA, Cir. ortop. y traumatol. **3**:141 (July-Sept.) 1935.

After studying in detail the principal causes of clubfeet Vianna presents a review of the treatment up to now and points out his own measures as carried out in the Hospital San Francisco de Asís in Rio de Janeiro. In general, the treatment to be employed depends on the age of the patient: Up to the age of 3, it should be manual setting; from 3 to 8, surgical intervention in the soft parts, and after 8, surgical intervention in the skeleton itself. He discusses the different surgical interventions used up to now, stressing those of Phelps-Kirmisson, Ombrédanne, Farabeuf, Nové-Josserand, Albee and others. He offers his own

method for treating bilateral congenital inverted clubfoot by a single operation. He calls it the "association procedure" and stresses that its aim is well defined and limited.

HERRON, Spokane, Wash.

EARLY TREATMENT OF CONGENITAL DISLOCATION OF THE HIP. G. HABERLER, München. med. Wchnschr. **83**:967 (June 12) 1936.

Haberler urges early nonsurgical treatment of congenital dislocation of the hip. The joint must be properly reduced and then immobilized with plaster of paris.

BRAHDY, Mount Vernon, N. Y.

ORTHOPEDICS DURING OFFICE HOURS OF THE GENERAL PRACTITIONER. MAGG-FELLHEIM, München. med. Wchnschr. **83**:1465 (Sept. 4) 1936.

The fate of a child who has the misfortune to have tuberculosis of a bone or joint depends on the early diagnosis of the condition. Luxation of the hip leads to crippling unless it is recognized early and treated. The treatment of clubfoot should start in the first few days of life. A rachitic scoliosis must be recognized in its early stages and proper therapy instituted.

Dislocation of the hip can be differentiated from coxa vara roentgenologically. When a child complains of pains in the knee, and no physical abnormality can be found in the knee, it is important to keep in mind the possibility of tuberculosis of the hip. Abdominal pain without objective findings in the abdomen should suggest the possibility of tuberculosis of the spine.

BRAHDY, Mount Vernon, N. Y.

CONGENITAL DISLOCATION OF THE HIP. FELIX BAUER, Wien. klin. Wchnschr. **49**:919 (July 17) 1936.

Bauer reports a method for the early diagnosis and treatment of congenital dislocation of the hip. His method has been tried, with good results, in sixty-two cases, including twenty-six of severe and thirty-six of partial dislocation. Of the former, twenty occurred in infants less than 1 year old and six in infants less than 2 years old.

Bauer has found that the development of the hip joint depends on two factors: (1) natural function of the joint with adequate motility and (2) normal fetal position in abduction. Fetal malposition may result in restriction of the motion or in dislocation of the joint, so that it is underdeveloped. Following a consideration of these factors, the natural functional method of treatment for underdevelopment or dislocation of the hip joint is considered. As soon as possible after birth, normal function and abduction must be sought. Complete fixation of the joint or, at the other extreme, no restriction at all, is to be avoided during the first year.

The functional treatment consists in early reduction without narcosis. A brace is applied which adequately protects against dislocation but permits considerable freedom of movement. The child crawls and learns to walk normally. Previous methods of treatment have aimed merely at mechanically keeping the joint in place. Its development was left for the future or disregarded. Bauer's method aims at anatomic improvement. He claims that the joint is rendered less susceptible to dislocation in half the time required by fixation methods. Early treatment is important. Complete or partial dislocation should be diagnosed by the fourth to eighth week of life. If treatment is begun early, the joint should be normally developed by the end of the first year except in cases in which there seems to be a hereditary disposition for the dislocation to be unusually severe, or in which the joint has been dislocated for some time prior to delivery. In such a case treatment must be continued during the second year of life.

One of the important causes contributing to dislocation of the hip is fetal malposition. Diagnosis of the latter condition often permits early diagnosis of dislocation. Fetal malposition usually results in increased development of one side of the body. The infant with such a condition usually prefers to lie on one side, and the skull is often asymmetrical.

ABT, Chicago.

## Miscellaneous

"IS PHENOLPHTHALEIN HARMFUL?" ZOLTÁN VON VAMOSSY, Am. J. Digest. Dis. & Nutrition **3**:22 (March) 1936.

Von Vamossy answers the criticism of phenolphthalein as a laxative. He describes the discovery of the laxative action of the drug, and its introduction in 1902 on the basis of experimentation with animals and observations on himself and his associates, and also on its clinical trial with a great many adults and children.

He cites many of the reactions attributed to the drug, but considers most of those reported as not definitely proved.

Von Vamossy admits that some persons have an allergic hypersensitiveness to phenolphthalein, which usually manifests itself in a mild cutaneous eruption. He contends that phenolphthalein is harmless.

MORRISON, Savannah, Georgia.

ABDOMINAL PAIN IN CHILDREN. R. M. SMITH, M. Clin. North America **19**:1603 (March) 1936.

The more important conditions, intra-abdominal and otherwise, responsible for abdominal pain in children are discussed. The necessity for careful history taking, examination and evaluation of symptoms even in urgent conditions is enjoined. Nor should the examination be limited to the abdomen. A complete physical examination is necessary, since such divers conditions as spinal disease, allergy, diabetes and purpura are possible causes of pain referred to this region.

The technic to be employed in reaching a correct diagnosis is outlined.

EUGENE SMITH, Ogden, Utah.

INFRA-RED IRRADIATION. W. ANNANDALE TROUP, Brit. J. Phys. Med. **10**:94 (Oct.) 1935.

Troup discusses the physiologic action, the apparatus and the technic of infra-red irradiation. He recommends it for sprains, painful conditions of the joints, including rheumatoid arthritis, and boils and carbuncles.

HARTMAN, Cleveland.

THE PRODUCTION OF INFRA-RED AND ULTRA-VIOLET RADIATION. B. D. H. WATTERS, Brit. J. Phys. Med. **10**:96 (Oct.) 1935.

The artificial and natural production of infra-red and ultraviolet radiation is discussed in a nontechnical and interesting article.

HARTMAN, Cleveland.

INHALATION TREATMENT. LEONARD HILL, Brit. J. Phys. Med. **10**:177 (Feb.) 1936.

Hill describes and illustrates several types of vaporizers and nebulizers.

HARTMAN, Cleveland.

DISEASE SIMILARITIES IN IDENTICAL TWINS. P. LEREBOULLET, Nourrisson **23**:341 (Nov.) 1935.

Several cases from Lereboullet's own practice are cited to show that identical twins often suffer from the same diseases synchronously and that in each pair the attacks tend to run parallel courses. Twin girls aged 16 months both had bronchopneumonia ; the temperature charts were almost identical, and after

illnesses of twenty-three and twenty-four days, they died within twenty-four hours of each other. Other striking examples are cited of twins simultaneously sick with (1) diphtheria, (2) congenital syphilis and (3) prematurity. Other cases, from the literature, included those of twins with (1) rheumatic ophthalmia, (2) hypertrophy of the thymus, (3) splenic anemia, (4) pulmonary tuberculosis, (6 Friedreich's ataxia, (6) multiple sclerosis, (7) congenital myatonia, (8) diabetes and (9) psychoses.

McCLELLAND, Cleveland.

RÔLE OF THE PHYSICIAN IN PHYSICAL EDUCATION AND SPORTS. GEORGES ROSENTHAL, Paris méd. **2**:101 (Aug. 8) 1936.

Rosenthal points out the necessity of medical examination before engaging in active physical exercise. This applies equally well to the child in school and to the adult engaging in sports. He points out particularly that the child handicapped through heart disease or other disturbances needs supervised exercise. In these cases close cooperation between the physician and the teacher of physical education is essential.

LESLIE, Evanston, Ill.

PHYSICAL EXERCISES FOR CONVALESCENT CHILDREN. H. ROUÈCHE, Rev. méd. sociale de l'enf. **3**:87 (March-April) 1935.

Not claiming to report any new idea, Rouèche mentions his experience with one hundred pretuberculous children at the Villemin pavilion under the supervision of René Marie, in 1910 and 1911. For one hour a day the children were given respiratory education by movements of the arms and legs and flexion of the trunk.

This beneficial type of exercise was continued during the war. Dr. Carton, medical associate of Brévannes, modified the technic and published his results in 1919.

After the war Rouèche, until 1925, had further experience with convalescent children of school age at a center of physical education at Bastion 42. He calls for a more general adoption of exercise during a child's convalescence.

SHAW, Evanston, Ill.

PHARMACOLOGIC STUDIES ON OIL OF CHENOPODIUM. LEONARDO DONATELLI, Pediatria **43**:161 (Feb.) 1935.

The author submits further results of his work directed toward determining the action of distillated products of oil of chenopodium. His present work represents a study on cold-blooded animals (frogs) and warm-blooded animals (guinea-pigs and rabbits). His detailed discussion is summarized in the following conclusive observations:

1. The actions of all preparations of oil of chenopodium are similar qualitatively but differ in degree.

2. Each preparation exhibits a distinct cardiac toxicity, manifested by hypotensive action.

3. Small doses arrest cardiac action in diastole, while greater concentrations act similarly in systole.

4. Because of their action on the respiratory center these preparations exhibit a marked stimulation of respiration in small doses, while larger doses inhibit respiratory action and lead to paralysis of the respiratory organs.

5. Each preparation exhibits a toxic action on the myocardium and a stimulating action on the vagus.

SIGNORELLI, New Orleans.

HEMOTHERAPY IN PEDIATRICS. A. BROSSA Y BOSQUE, Paidoterapia **14**:1023 (March) 1936.

Brossa y Bosque includes a historical review and an account of technic in use up to the present day. He points out the characteristics of the blood groups in

infants, the technic of transfusion, the quantity of blood to inject, the ways of access to the veins and the incidents and accidents of the procedures. He summarizes studies of indications which present themselves in pediatrics, as following hemorrhages, anemias, infections nutritional troubles, congenital weakness, prematurity, traumatic and operative shock, grave burns and intense chemical intoxications. He gives a helpful general review of studies of hemotherapy and of the indications for its use in pediatrics.

HERRON, Spokane, Wash.

PUBERTY AND ILLNESSES RELATED THERETO. ERNO DEUTSCH, Paidoterapia **14**: 1123 (April) 1936.

Deutsch describes the physiologic findings in the boy and girl who reach the age of puberty. He goes into detail on the changes that occur just before puberty, during the pubertal period and in the period of full sexual development, in the boy and in the girl. Not only are the anatomic changes discussed but the mental and the pathologic changes. A special chapter is devoted to the psychopathies, juvenile criminality, and the difficulties of the after the war youth. He insists in detail on the obligations of parents, teachers, clergymen, doctors and judges to youth. In a special chapter he gives the recreations, both physical and mental, for this type of youth. He criticizes the use of alcohol and smoking. A good discussion on the glands of internal secretion is a feature.

HERRON, Spokane, Wash.

HYPERTROPHY OF THE CHROMAFFIN SUBSTANCE OF THE ADRENAL GLANDS IN CHRONIC CARBON MONOXIDE POISONING. F. J. SCHMELZER, Arch. f. Hyg. **115**:1 (Oct.) 1935.

The effect of acute, subacute and chronic carbon monoxide poisoning on the adrenal glands of guinea-pigs was studied. In the experiments on acute poisoning the animals were killed by 5 or 10 per cent of the gas in air in periods of from 15 to 30 minutes. Acute poisoning caused a diminution of the chromaffin material of the adrenal glands. In subacute poisoning the animals inhaled 0.8 per cent of carbon monoxide for one-half hour every other day and were killed at intervals varying up to twenty-four days. In the chronically poisoned animals carbon monoxide gas varying in strength from 0.25 per cent to 0.5 per cent was administered at various intervals for periods lasting as long as six months in some cases. Subacute poisoning resulted in findings similar to those produced by chronic poisoning. In this condition there were a marked anatomic hypertrophy and physiologic overactivity of the medullary cells of the adrenal glands.

GLASER, Rochester, N. Y.

ULTRAVIOLET RAYS IN THE EXPERIMENTAL TREATMENT OF CARBON MONOXIDE POISONING. W. ESTLER, Arch f. Hyg. **115**:152 (Dec.) 1935.

Estler reviews the literature concerning the effect of light on the dissociation curve of carbon monoxide and hemoglobin. While the reaction obtained in vitro is in favor of an accelerating reaction, he was unable to show that ultraviolet ray treatments were of any value to rabbits poisoned by carbon monoxide.

GLASER, Rochester, N. Y.

AIMS AND SIGNIFICANCE OF CHILDREN'S HOSPITALS. HERBERT KOCH, Wien. klin. Wchnschr. **48**:1375 (Nov. 8) 1935.

Koch sketches the history of children's hospitals and shows how their services have gradually become broader and more manifold. The modern institutions developed out of foundling asylums, in which there was a high rate of morbidity and mortality. The special care of infants and children was not understood, and the simplest measures of modern hygiene were unknown. As time passed,

the foundling asylums, which were at first private institutions and did not have any special aid, began to turn to physicians for help. Public support began to replace private initiative. When the first children's hospitals were founded, it was not felt that children required care essentially different from that given adults. The experiences of doctors in connection with the children's hospitals soon made it clear that diseases in the early period of life require special study and special care and treatment. The institutions began to devote more and more time to research. As knowledge grew, pediatrics began to be differentiated more and more from internal medicine and diseases of women and children, though it has always maintained close connection with these branches. The ideal director of a children's hospital should know all branches of medicine, though this cannot be realized in practice.

The modern children's hospital is often a center of infant welfare and preventive pediatrics. It provides for the care and treatment of sick children and offers facilities for the training of medical students and nurses. It often presents opportunity for research and occupies an important place in the field of public welfare.

ABT, Chicago.

MEDICAL EXAMINATION OF STUDENTS. EDWARD NEUBER, Wien. klin. Wchnschr. **49**:907 (July 17) 1936.

Neuber presents the results of an examination of 265 first year high school students at the Tisza István University in Debrecen. Of these students, 0.37 per cent suffered from active, 6.03 per cent from inactive, pulmonary tuberculosis. Cardiac changes could be established in 10.9 per cent by physical methods and in 16.9 per cent roentgenologically; 5 students (1.9 per cent) were found to have organic heart disease. The necessity of examining the urine is clearly shown by the fact that varied positive findings were made in 5.1 per cent of the students.

A surgeon examined the young men. He found that 135 of them had congenital anomalies and showed severe or minor anatomic lesions, and that some students suffered from more than one irregularity; that is, over half were not "passed" by the surgeon. Some of the more important findings were: severe flatfoot in 54 patients; moderate flatfoot in 28; severe spinal malformations in 4 and moderate spinal malformations in 11.

The findings may be distributed into four groups as follows:

1. Anomalies which have a permanent effect on the ability of the student and which cannot always be improved by long treatment or operation. The severe spinal malformations belong in this category. One student was found to be suffering from active tuberculosis and had to be withdrawn from school immediately. Orthopedic measures were instituted to help the young men suffering from severe flatfoot.

2. Disorders which do not cause any immediate difficulty but which must be treated if later trouble is to be avoided: moderate spinal malformations, moderate flatfoot, inguinal hernia, hydrocele and other disorders. Any of these conditoins may, in the long run, severely incapacitate the student.

3. Earlier disorders or those resulting from other illnesses such as effects of previous operations, atrophy of the testicles and fractures which have not healed properly.

4. Developmental anomalies, which may be insignificant or, on the other hand, may lead to severe complications. Here belong various bone and joint disorders, including arthritis. Some of these cannot be cured unless the patients change their entire mode of life.

An important conclusion which Neuber draws from this investigation is that the majority of the students had no previous knowledge of their ailments. Those suffering from flatfoot continually took part in sports which were harmful. The student suffering from tuberculosis had already been ill for two years but had not rested at all. Several of the students suffering from hernia or spinal malformation had no adequate conception of their condition.

ABT, Chicago.

ISOLATION OF INFANTS BY PIRQUET'S METHOD. EDMUND NOBEL, Wien. klin. Wchnschr. **49**:1020 (Aug. 14) 1936.

Nobel states that when infants are quartered in the same room of a hospital there is always danger of cross-infection. The danger is especially great if the infants are premature or new-born. In 1928 Pirquet attempted to solve this problem by building special beds with glass walls. Since single beds proved too expensive, groups were constructed. For eight years this method of isolation has been tried at the Vienna Children's Clinic and the Mautner-Markhof Children's Hospital in the same city. Access to each compartment may be had by a glass window. The glass walls are high so that the spray from a cough or a sneeze cannot enter a neighboring compartment. The mattress lies on a frame which can be raiscd or lowered at each end of the bed so that the desired position can be obtained—for example, when the baby is to be fed. The question is often asked whether the infants obtain sufficient air in these apparently closed glass boxes. Experience has shown that the ventilation is quite satisfactory. The temperature in the boxes is usually the same as in other parts of the room. Although the glass beds are expensive they have the advantage that a greater number of infants can be quartered in a single room. The isolation beds allow the placing of eight infants in a room previously intended for five.

Eight years of experience have shown that the Pirquet isolation beds are an ideal solution of the problem of infant hospitalization. Cross-infections are prevented, and experienced physicians know how important this is, especially in children's hospitals.

ABT, Chicago.

CARCINOMA AT EARLY AGES. H. ROSENBERG, Ztschr. f. Krebsforsch. **41**:230, 1934.

In a study of cases of juvenile cancer observed at the Pathologic Institute of Munich during the years from 1910 to 1933, 81 cases, 2 per cent of all the cases of cancer during this period, were observed. The disease involved principally the gastro-intestinal tract. Cancer of the female genital organs was rare under the age of 25 years, but in the period from 26 to 30 years it was almost as frequent relatively as in later life. Diagnostic errors were little more frequent in these cases than in those occurring at later ages. Nothing could be noted to indicate exceptional malignancy of the early cancer. Cohnheim's theory was applicable only rarely.

EGGERS, Omaha. [ARCH. PATH.]

# Society Transactions

## CHICAGO PEDIATRIC SOCIETY

*Regular Meeting, Dec. 15, 1936*

ROBERT A. BLACK, M.D., *President*

SOME OBSERVATIONS ON THE EPIDEMIOLOGY OF CERTAIN STREPTOCOCCIC DISEASES. DR. JOHN HAYS BAILEY (by invitation).

An epidemic of scarlet fever in a city with a population of about 20,000, in the western part of Illinois, offered an excellent opportunity to study the transmission of this disease. The first case was not reported as one of scarlet fever, but the boy in the case returned to school with suppurative otitis media. Within three weeks after he returned to school, 39 cases of scarlet fever had developed among the 325 pupils of that school. The situation in the rest of the city and in a contiguous city was normal for that period of the year. Immunization with scarlet fever streptococcus toxin was considered, but it was felt that the consent of a sufficient number of parents could not be obtained to make the procedure effective.

All the children present in school on a certain Monday morning had their throats swabbed for hemolytic streptococci, and it was found that 45 per cent of them harbored these organisms. The school authorities agreed to run the school in two shifts, keeping the carriers and the noncarriers separated so far as possible, and, as a consequence, no more scarlet fever appeared in that school. The carriers were followed by means of cultures for about a week, and after two consecutive negative cultures had been obtained, they were allowed to return to the other group. A few of them continued to be vectors of hemolytic streptococci for a considerable period.

On careful tests and investigation of air currents in the school room it appeared likely that the disease was transmitted from carriers, one of whom was the lad who presented the original case, by droplets carried on the air currents from the rear of the room forward. From these observations it seemed logical to assume that the spread of infection might be controlled by placing the persistent carriers in the front seats. This change of seating was made and to all appearances was a completely satisfactory method of handling persistent vectors in a school room.

The drinking fountains also were investigated. A sample of water was taken from one of them during the middle of a class period. Immediately afterward one of the known carriers was asked to drink at that fountain, and then a second sample was taken. The first specimen showed no hemolytic streptococci, but the second sample teemed with them. Drinking fountains of this type are not now permitted in new buildings.

Streptococcus haemolyticus causes mortality in all periods of life. The cause of much of the mortality in the two extremes of life is designated as erysipelas, and that in between, as scarlet fever. Is it not possible that scarlet fever and erysipelas are the same disease? Mortality statistics show that they occur in inverse proportion: When deaths from erysipelas increase, deaths from scarlet fever decrease. The relationship of the two diseases is further emphasized if the percentages of all deaths from them occurring in each month are compared. There is a steady rise in both from September to January, when a plateau is reached, but a peak occurs in March with a gradual fall to May, after which the decline is more pronounced. Other contagious diseases, for instance, measles and diphtheria, have individual patterns in no way resembling that of the two streptococcic diseases, for scarlet fever and erysipelas follow an almost identical pattern.

No final and complete proof for the ideas expressed here can be given at this time, but it is hoped that these observations will serve as a stimulus to further thought and experimentation by others.

DISCUSSION

DR. ARCHIBALD HOYNE: There is an outstanding fact that this paper emphasizes—the importance of carriers in outbreaks of scarlet fever. In this respect scarlet fever is not different, possibly, from diphtheria. The present system of control of scarlet fever through quarantine is unsatisfactory.

When the child cited returned to school with a discharging ear, he may have been responsible for the spread of scarlet fever as suggested. On the other hand, spread of the infection could have been due to another carrier in the school. One has been accustomed to believe that scarlet fever is purely a matter of contact. If the carriers in the back of the room traveled to the front of the room for the purpose of making recitations, I do not see why contact could not explain the development of scarlet fever in the cases in which it occurred. Nevertheless when the carrier sneezes or coughs, he might very easily transmit scarlet fever to a susceptible person in the same room even though the latter was some distance away.

Generally when a child leaves the hospital at the end of the period of quarantine, if there have been no complications there is no fear of contagion. But my associates and I attempted to show, a few years ago, that the patient who has complications is not the one who most frequently transmits scarlet fever after returning home. The explanation is that the child who has had complications is feared by the family, and every possible precaution is taken to prevent transmission of any condition he has to members of the family; whereas on a child's recovery from so-called mild or uncomplicated scarlet fever he is embraced by all members of the family; organisms may be present in this child's nose and throat, and a susceptible contact may acquire the disease.

Consider the attitude toward the patient in the hospital: The period of quarantine is twenty-eight days, during which time the patient's disease is regarded as contagious. But just as soon as the clock strikes the hour of twelve on the last day, the patient is "free from contagion" and goes home. Physicians do not release patients who have had diphtheria that way, and medical authorities will not be able to control scarlet fever until improved methods are developed. A satisfactory plan for active immunization would be a great help.

I do not believe that erysipelas and scarlet fever can be regarded as the same disease. Occasionally one has patients who have both diseases at the same time. Of course, the suggestion can be made that one is purely an infection of the skin. However, in many features the diseases differ.

I think Dr. Bailey has shown many interesting things in this study, particularly in regard to carriers. Medical authorities cannot control scarlet fever by the measures now commonly adopted. Yet any outbreak of scarlet fever can be checked by the isolation of all carriers of hemolytic streptococci as well as of those who have scarlet fever.

DR. JOSEPH BRENNEMANN: My colleagues and I have had experience with a certain phase of this subject in the Children's Memorial Hospital that may be of interest to the members. The hospital is made up of a number of pavilions. It is our experience that we almost never see a case of scarlet fever secondary to one in which there has been the classic picture of scarlet fever with a rash. Isolated cases crop out anywhere in the hospital without any relation to a former case in which scarlet fever has been diagnosed. There are rather obviously two sources of infection: a carrier among the hospital personnel, and a child who gives one every reason to believe that he has a rashless scarlet fever. If every member of the hospital personnel who harbors a few hemolytic streptococci in his nose or throat were isolated, there would be times when physicians of the staff would be compelled to stop functioning. The child who has the appearance of scarlet fever except that there is no rash will not be accepted by a hospital for contagious diseases, nor do we feel justified in transferring him to our limited pavilion for contagious diseases. Directly or indirectly he becomes a factor in the transmission of the disease to another person. It is this that makes the situation with regard to scarlet fever in a children's hospital, as Dr. Hoyne has

stated, all but hopeless at the present time. It is in this respect that scarlet fever bothers us more than all other contagions.

I do not believe that erysipelas is the same as scarlet fever, nor do I believe that every slightly spreading streptococcic dermatitis should be called or treated as erysipelas, and I do not think that the hazard from true erysipelas is anything like that from a throat infection due to hemolytic streptococci.

DR. MAURICE L. BLATT: How many colonies of hemolytic streptococci on a plate are necessary before a person is to be considered a carrier?

DR. LLOYD ARNOLD: I do not know that I can speak of scarlet fever before pediatricians—those present here have seen much more than I have. Dr. Bailey has been working in my laboratory for a couple of years. There is one aspect outside this new interpretation of scarlet fever, and that is atmospheric pollution, one might say, the transmission of infections, including the streptococcic, of the upper respiratory tract. It is quite evident that one confronts here a pathway of transmission of scarlet fever not only from patients but from carriers. I am interested in atmospheric pollution. Many consider water pollution, food pollution, etc., as significant and get worked up about it, demanding certain requirements that must be adhered to in all these various environmental factors, but as for atmospheric pollution many seem to think it does not occur. The distribution of streptococci in the atmosphere is the most interesting phase, to me, of the problem presented by Dr. Bailey.

DR. J. A. BIGLER: I should like to ask Dr. Bailey if he took cultures on successive days from the same patient.

When my associates and I took cultures for ten days on the same persons, we found marked variations. There might be forty with positive cultures on the first day. There might be forty on the second day, but many persons who gave positive cultures the first day might give negative ones on the second day, and many who gave negative cultures on one day were found with positive cultures on the next. We found the percentages of the cultures according to the numbers of colonies on plates and found that the number of colonies present varied widely for the various persons from day to day.

DR. JOHN HAYS BAILEY: In reply to Dr. Blatt: A swab is rubbed over the tonsil, and a plate is inoculated and streaked with the material. If one could grind up the tonsil and make an emulsion of it, the number of colonies on the plate might mean something. The important thing is: Are there any hemolytic streptococci there? The negative culture does not mean as much as the positive.

Dr. Bigler brought up a very pertinent point. Unfortunately my associates and I were able to be there only one day. I am well aware of the fact that carriers will disappear, and I wonder if it is a true disappearance or if it is due to a fault inherent in the technic.

As for erysipelas and scarlet fever being the same, I am sorry I left that impression. I meant that they were merely different manifestations of the same infection. They are caused by identical organisms. If a sufficiently large number of cases were examined, this would be found to be so. I cannot prove it, although feel that erysipelas and scarlet fever are the same infection.

CLINICAL OBSERVATIONS ON GRIP AS SEEN IN PEDIATRIC PRACTICE. DR. C. A. ALDRICH.

A method of keeping records of diseases and their complications as seen in private practice is described. Such records in 1,146 cases of grip occurring between February 1930 and January 1936 form the basis of this report. The symptoms of grip and the diagnosis criteria are outlined.

During this period, grip occurred in yearly epidemics of considerable proportions except in the winter of 1933-1934, when there was an obvious but much smaller wave.

Laryngitis or croup occurred in smaller epidemics identical in time with those of grip, making it seem probable that croup is a manifestation of grip in infancy.

The epidemics of grip showed no chronological relation to the prevalence of general respiratory disease as shown by comparison with the incidence of pharyngitis.

The disease attacked children of all ages. The complications were tabulated and it was demonstrated that otitis media and capillary bronchitis were by far the most common.

Of the children who had capillary bronchitis, 70 per cent were known to be asthmatic, and another 17 per cent were probably allergic. This raises the question as to whether or not the physical findings leading to the diagnosis of capillary bronchitis were not due to an allergic reaction in the bronchi.

Complications conspicuous by their absence were endocarditis, empyema, nephritis, pyuria and arthritis. It is evident that these conditions are not usually caused by grip.

The prognosis was extremely good. The only death was from meningitis, which resulted when measles complicated grip with associated mastoiditis.

DISCUSSION

DR. H. E. IRISH: I should like to express my extreme pleasure in hearing the presentation of a study of such great proportions and such apparent accuracy in details. It almost takes one back to the horse and buggy days to hear an actual description of different symptoms in detail with definite relationship to what is to follow. One ought to feel impressed to know that there is some substitute for the more or less messy habits doctors get into with regard to clinical observation, awaiting the results of cultures or smears or the use of some mechanical aid. This paper ought to give a stimulus in the direction of more accurate clinical observation.

DR. JOSEPH BRENNEMANN: McKenzie in his smaller book, "The Heart," makes the statement: "Medicine will make but halting progress until the general practitioner becomes also the investigator in medicine," and all know how he exemplified that fact. The hospital ward and the laboratory are not the only places where investigation can be carried on. A lot can be learned in private practice. I always tell interns and residents that there will be much for them to learn about medicine when they get into practice and also something to forget of what they learned in the hospital. It is for all these reasons that this paper, so carefully and laboriously worked out, has an especial appeal. It substitutes statistical information for mere impression.

One's appreciation of a paper is not lessened because one differs with some of its conclusions in minor respects. I am not sure that I have ever acquired the ability to recognize grip in the present sense as a separate entity. I have too many times seen in the same family one person with a mere cold, another with a sore throat and possibly an involved ear, and the third with what would clearly come in the category of what Dr. Aldrich calls grip; and yet I believe that all the conditions have an identical etiology as far as the causative organism is concerned. For that reason, I have contented myself with using such expressions as "throat infection" and "grippy infection," and I have often wished that I had some short word that I could use to designate this whole group of infections instead of so cumbersome an expression as "infection of the upper respiratory tract" or such limiting terms as "tonsillitis" or "pharyngitis" or, again, such questionable terms as "influenza" or "flu" or "grip." The Germans have a way of calling all of these things *die Grippe*. I have often thought that "the grip" would be a good term to use were it not for the memories that still linger of the grip in 1918-1919. The present paper, too, casts doubt on the wisdom of that designation for all these infections.

I should question a little, too, the use of the expression "capillary bronchitis" to designate those localized fine crackling râles that one so often finds at the base of the lung in these conditions. "Capillary bronchitis" has come to mean a fairly definite clinical entity in which there are fine crackling râles all over the chest

and which has a rather serious prognosis. It seems to me that the most one could say is that there is localized capillary bronchitis or bronchiolitis.

I was especially interested in the frequency with which laryngitis and asthma occurred in this series. One of the important contributions of a paper of this kind is to point out the actual incidence of disease, which, of course, the hospital ward does not do.

DR. C. A. ALDRICH: I wish to thank Dr. Brennemann for his very kind remarks. With reference to the term "capillary bronchitis," when I was a student I was told that this disease was desperately serious. I have never seen fatal capillary bronchitis in private practice. If somebody would offer a better term I should be glad to use it.

"Infection of the upper respiratory tract" is an inaccurate term for doctors to use, particularly pediatricians. If doctors could get into the habit of making a diagnosis of what they see rather than lumping everything under "infection of the upper respiratory tract," they would be much clearer in their thinking. Only when I began charting the symptoms did I see this clear picture of grip. I noted that it was not an evident infection of the upper respiratory tract at the onset but was characterized by fever and chill, with respiratory symptoms later. I should be very glad to second Dr. Brennemann's motion that doctors scrap the term "infection of the upper respiratory tract."

THE LYTIC INDEX OF HUMAN MILK AND ITS RELATIONSHIP TO THE BACTERIAL COUNT. DR. MAURICE L. BLATT.

This article is published in full in this issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN, page 767.

# Book Reviews

**Die Wirkung der Rohobstdiät auf den kindlichen Organismus.** By Dr. Theophil Baumann. Reprinted from volume 42 of "Abhandlungen aus der Kinderheilkunde und ihren Grenzgebieten." Price, 4.20 marks. Pp. 155, with 34 tables. Berlin: S. Karger, 1936.

The author presents the results of an exhaustive study of the effect of raw fruit diets in children. The subject matter is divided into three parts: (1) the results of his clinical and experimental investigation of the various substances in raw fruit that might be concerned and their behavior in the gastro-intestinal canal; (2) the results of an investigation of the organic and inorganic metabolism of infants and of older children on raw fruit diets, including also the results of an investigation of hunger metabolism in the growing organism, and (3) clinical experiences in the treatment of acute intestinal disturbances in childhood by means of raw fruit diets.

The author's historical review of the subject shows that the beneficial effect of raw fruit diets on diarrheal conditions has been attributed by various clinicians to several factors but that they assigned the chief rôle to maleic acid, to pectin or to tannic acid. The author analyzes the physicochemical composition of apples and of bananas and the chemistry of pectin and gives a detailed report of his experimental studies of the mechanism by which a raw fruit diet affects the gastro-intestinal canal. He discusses the degree of acidity, the influences exerted by pectin, the effect of raw fruit on the mechanics of the intestinal canal, the effect of cellulose, the effect of tannic acid, the influence of raw fruit on the flora of the stools and the absorptive power of pectin, and he gives a critical analysis of the stools of children on a raw fruit diet.

One whole chapter is devoted to investigations of the hunger metabolism of the growing organism as related to the raw fruit diet, and it contains a careful and clear analysis of the author's results.

Some of the author's conclusions concerning the manner in which raw fruit diets work can be summarized in the following way: Raw fruit diets (banana and apple) have a favorable therapeutic influence in the cure of intestinal diseases because they possess the properties common to all therapeutic foods and also specific properties peculiar to raw fruit. The essentials common to all therapeutic foods are met by a raw fruit diet because it is at once a one-sided diet (excess of carbohydrate, slight protein content, minimal amount of fat, excess of potassium and decrease in the calcium, sodium, phosphorus and chlorine content), a starvation diet (low caloric content) and a diet of fine colloidal dispersion. These three general properties effect in the gastro-intestinal canal a change of flora, a state of rest and an easy digestibility that diminishes stagnation.

In addition to these three properties, common to all curative foods, the raw fruit diet possesses properties peculiar to it alone. Most important and of greatest practical therapeutic influence is pectin. Its therapeutic effect is primarily due to its physical property of marked ability to swell and to absorb. Pectin works particularly well in its natural combination as a cement substance with the cellulose of fruit. The administration of chemically pure pectin dissociated from the cellulose, on which it is most dependent for its therapeutic effect, does not give the favorable results obtained from raw fruit. Because of the coarsely voluminous nature of the ingesta and of the stools resulting in an increase in the distention of the intestines and an increase in stimulation by the coarse particles of cellulose, the raw fruit diet causes stronger peristalsis and thereby an acceleration of the time of passage; but in spite of this acceleration the bowel is completey emptied and no stagnant residue is left. The marked swelling and absorptive properties bring about a mechanical cleansing of the gastro-intestinal canal. An increase in the lymph flow occurs and also absorption of bacteria and probably of toxic metabolic products, which are carried out in the "raw fruit cast" of the intestinal

canal. With every acute, subacute or chemical digestive disturbance or intestinal disease there is the fear that with acceleration of peristalsis there will be local stagnation of ingesta and consequent bacterial invasion of the upper portions of the intestines and qualitative and quantitative overproliferation of pathogenic bacteria. The peculiar properties of pectin, together with the entire structural characteristics of raw fruit, diminish greatly the factors that make such a state of affairs possible.

The author's clinical experience with raw fruit diets in the treatment of acute and subacute intestinal disturbances and the impressions gained from the recorded experiences of others lead him to certain conclusions, some of which are of especial interest. Raw fruit treatment in the first nine months of life offers no advantage over the older types of therapy with adequate therapeutic food except that in the treatment of celiac disease at this age the banana diet has great value.

In later infancy and in early and later childhood the raw fruit treatment of acute and subacute disturbances of the bowel shows a definite superiority over the customary methods of treatment.

Satisfactory results will be obtained only if a definite procedure is insisted on. The author suggests from six to twelve hours of tea alone and then from three to four days of raw fruit and tea sweetened with saccharin. After this the transition to a normal diet should take two, three or four days, depending on the severity of the illness.

Bananas are preferred in most cases for several reasons. The high caloric value eliminates the precipitous loss of weight seen with apple diets, and the softer cellulose of bananas eliminates the too marked irritation of the mucosa of the bowel which is sometimes seen with apple diets.

This monograph is a thorough and clear presentation of the subject, and any physician interested in the treatment of intestinal disturbances could find no more comprehensive review of the present knowledge of the raw fruit treatment than that presented here.

**Die Neurosen des Kindes-und Jugendalters.** By Walter Cimbal. Second edition. Price, 13.50 marks. Pp. 490. Berlin: Urban & Schwarzenberg, 1935.

By definition the disorders considered in this work are psychobiologic disharmonies of childhood and adolescence, not permanent and irreversible defects. As such they are amenable to treatment by psychotherapeutic or medical measures or both, numerous rules and plans for the various syndromes being given.

The book is arranged systematically into a section on general pathology, a section on special pathology and one on treatment, general and special. In the first part a theory of the neuroses of childhood is propounded, partly on psychoanalytic lines. The question of character formation is considered under the heads of inherent constitutional traits, chance environmental factors, natural developmental stages and crises, and what is noteworthy and commendable in any treatment of this subject, an attempt is made to relate the knowledge of internal metabolism to normal and abnormal character formation. There are chapters also on training of the moral sentiments and of concrete thinking. Cimbal draws to a large extent on his own experience and knowledge in forming his generalizations and conclusions. This is well, but may account for a certain regrettable dogmatism in the theoretical sections on many points better left open.

Of the special syndromes those of defects in learning performance and behavior disturbances receive the most attention, commensurate with their great frequency in the sum total of neuroses in children. Neurasthenia, hysteria, convulsive states, disturbances of speech, disorders of movement, visceral syndromes, congenital syphilis and the psychoses all have their chapters. Thus the work spreads so as to become a sort of textbook of the psychopathology of childhood and is rendered unsuitable for a short review. In the final section on treatment much space and attention are given to the orthodox matters of diet, climate and physical therapy and to involved medication and relatively less to psychotherapy.

# Directory of Pediatric Societies

## INTERNATIONAL

### International Association of Preventive Pediatrics

President: Professor G. Scheltema, 6a Herreplein, Groningen, Netherlands.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

### International Congress of Pediatrics

President: Prof. Luigi Spolverini, Policlinico Lungo Tevere Melini, 24, Rome, Italy.
Secretary: Professor Vitetti, Rome Italy.
Place: Rome, Italy. Time: Sept. 27-30, 1937.

American Committee:
Chairman: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary: Dr. L. Emmett Holt Jr., Johns Hopkins Hosp., Baltimore.

### International Congress for the Protection of Children

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.
Place: Rome, Italy. Time: Oct. 4-8, 1937.

## FOREIGN

### British Paediatric Association

President: Dr. Leonard Findlay, 14 Wimpole St., London, W. 1.
Secretary: Dr. Arthur G. Maitland Jones, 31A Weymouth St., London, W. 1.

### Paediatrický Spolok na Slovensku

President: Dr. A. J. Chura, Lazaretská 6, Bratislava, Czechoslovakia.
Secretary: Dr. S. Limbacher, Dlhá 2, Bratislava, Czechoslovakia.
Place: Pediatric Clinic, University, Bratislava. Time: Six times a year.

### Royal Society of Medicine, Section for the Study of Disease in Children

President: Sir Lancelot Barrington-Ward, 85 Harley St., London, W. 1.
Secretary: Dr. K. H. Tallerman, 122 Harley St., London, W. 1.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:30 p. m.

### Palestine Jewish Medical Association, Section of Physicians of Children's Diseases

President: Prof. S. Rosenbaum, 26 Bialikstr., Tel Aviv, Palestine.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv, Palestine.

### Sociedad Cubana de Pediatría

President: Prof. Félix Hurtado Galtés, Carlos III, 7, Havana.
Secretary: Dr. Carlos Hernández Miyares, San Lazaro 370, Havana.
Place: Cátedra de Clínica Infantil, Hospital Mercedes, Havana. Time: Third Thursday of every month.

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* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

## NATIONAL

### American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. Ralph M. Tyson, 255 S. 17th St., Philadelphia.
Secretary: Dr. Albert D. Kaiser, 16 N. Goodman St., Rochester, N. Y.
Place: Atlantic City, N. J. Time: June 7-11, 1937.

### American Academy of Pediatrics

President: Dr. Laurence R. DeBuys, 1417 Delachaise St., New Orleans, La.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Place: Waldorf-Astoria Hotel, New York. Time: June 3, 4 and 5, 1937.
Region I. Place: Boston, Mass. Time: Nov. 12-13, 1937.

### American Hospital Association, Children's Hospital Section

President: Mr. Robert Witham, Children's Hospital, Denver.
Secretary: Miss Agnes O'Roke, Kosair Crippled Children's Hospital, Louisville, Ky.

### American Pediatric Society

President: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid St., St. Louis.
Place: University, Va. Time: April 29-30 and May 1, 1937.

### Canadian Society for the Study of Diseases of Children

President: Dr. A. P. Hart, 1844 Bloor St., W., Toronto, Ont.
Secretary-Treasurer: Dr. Pearl Summerfeldt, Hospital for Sick Children, Toronto, Ont.

### Society for Pediatric Research

President: Dr. Francis Scott Smyth, University of California Medical School, San Francisco.
Secretary: Dr. A. A. Weech, 3975 Broadway, New York.
Place: Chalfonte-Haddon Hall, Atlantic City, N. J. Time: May 4, 1937.

## SECTIONAL

### North Pacific Pediatric Society

President: Dr. D. M. Dayton, Medical Arts Bldg., Tacoma, Wash.
Secretary: Dr. H. T. Clay, Medical Arts Bldg., Tacoma, Wash.
Place: Portland, Ore. Time: June 1937.

### Southern Medical Association, Section of Pediatrics

Chairman: Dr. Gilbert Levy, 20 S. Dunlap St., Memphis, Tenn.
Secretary: Dr. Hughes Kennedy Jr., Highland Plaza Apts., Birmingham, Ala.

## STATE

### Alabama Pediatric Society

President: Dr. Wallace A. Clyde, Employees' Hospital, Fairfield.
Secretary-Treasurer: Dr. M. G. Neely, Employees' Hospital, Fairfield.
Place: Birmingham. Time: April 19, 1937.

### Arkansas State Pediatric Association

Chairman: Dr. A. C. Kirby, 701 Main St., Little Rock.
Secretary: Dr. Madeline M. Melson, 909 Main St., Little Rock.

### California State Medical Society, Section on Pediatrics

Chairman: Dr. Edward B. Shaw, 384 Post St., San Francisco.
Secretary: Dr. E. Earl Moody, 3780 Wilshire Blvd., Los Angeles.

### Florida State Pediatric Society

President: Dr. Luther W. Holloway, 117 W. Duval St., Jacksonville.
Secretary: Dr. Warren W. Quillian, 227 Avenue Aragon, Miami.
Place: Concurrent with state association meeting at time of convention.

### Georgia Pediatric Society

President: Dr. Mercer Blanchard, 1301 Broadway, Columbus.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St., N. E., Atlanta.

### Indiana State Pediatric Society

President: Dr. Ernest R. Carlo, 2902 Fairfield Ave., Fort Wayne.
Secretary-Treasurer: Dr. Mathew Winters, 23 E. Ohio St., Indianapolis.
Time: Two meetings a year.

### Louisiana State Pediatric Society

President: Dr. Edwin A. Socola, 2000 Tulane Ave., New Orleans.
Secretary-Treasurer: Dr. Ruth Aleman, 1407 S. Carrollton Ave., New Orleans.

### Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. George M. Retan, 459 James St., Syracuse.
Secretary: Dr. John D. Craig, 33 E. 61st St., New York.

### Michigan State Medical Society, Pediatric Section

Chairman: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Secretary: Dr. C. R. Dengler, 131 W. Michigan Ave., Jackson.

### Mississippi State Pediatric Society

President: Dr. Harvey F. Garrison, 319 E. Capitol Pl., Jackson.
Secretary-Treasurer: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Place: To be designated by Society. Time: Yearly.

### Nebraska Pediatric Society

President: Dr. J. A. Henske, 1614 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. J. H. Murphy, 915 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

### North Carolina Pediatric Society

President: Dr. Leroy J. Butler, 405 N. Spring St., Winston-Salem.
Secretary: Dr. C. A. Street, 405 N. Spring St., Winston-Salem.

### Oklahoma State Pediatric Society

President: Dr. B. H. Nicholson, 301 N. W. Twelfth St., Oklahoma City.
Secretary: Dr. Hugh C. Graham, 1501 S. Baltimore Ave., Tulsa.
Place: Tulsa: Time: May 10-11, 1937.

### Pennsylvania Medical Society, Pediatric Section

Chairman: Dr. Joseph Stokes, Children's Hospital, Philadelphia.
Secretary: Dr. Theodore O. Elterich, 310 Medical Arts Bldg., Pittsburgh.

### South Carolina Pediatric Society

President: Dr. Leland B. Salters, 317 S. Warley St., Florence.
Secretary-Treasurer: Dr. D. Lesesne Smith Jr., 187 Oakland Ave., Spartanburg.

### Tennessee State Pediatric Society

President: Dr. Joe T. Smith, 702 Medical Arts Bldg., Knoxville.
Secretary: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.

### Texas Pediatric Society

President: Dr. George B. Cornick, 507½ E. Houston St., San Antonio.
Secretary-Treasurer: Dr. F. H. Lancaster, 1507 Medical Arts Bldg., Houston.

### Virginia Pediatric Society

President: Dr. Basil B. Jones, 1028 W. Franklin St., Richmond.
Secretary: Dr. W. A. McGee, 616 W. Grace St., Richmond.

### West Virginia State Medical Society, Section on Pediatrics

President: Dr. John T. Thornton, 58, 16th St., Wheeling.
Secretary: Dr. Claude L. Holland, 400 Locust Ave., Fairmont.

## LOCAL

### Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. J. D. Pilcher, City Hospital, Cleveland.
Secretary: Dr. William M. Champion, 2323 Prospect Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

### Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. T. B. Verner, 170 St. George St., Toronto.
Secretary: Dr. D. V. Hutton, 170 St. George St., Toronto.

### Bronx Pediatric Society

President: Dr. Daniel J. Dolan, 420 E. 159th St., New York.
Secretary: Dr. Samuel T. Levethan, 254 E. 184th St., New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

### Brooklyn Academy of Pediatrics

President: Dr. Thurman B. Givan, 115 Remsen St., Brooklyn.
Secretary: Dr. John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

### Central New York Pediatric Club

President: Dr. Frank Vasder Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Thursday of April and September.

### Chicago Pediatric Society

President: Dr. Robert Black, Del Prado Hotel, Chicago.
Secretary: Dr. James H. Wallace, 715 Lake St., Oak Park, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, inclusive.

### Dallas Pediatric Society

President: Dr. John Young, 3930 McKinney Ave., Dallas, Texas.
Secretary-Treasurer: Dr. John E. Ashby, 3622 Fairmount Ave., Dallas, Texas.
Place: Bradford Baby Hospital. Time: 1 p. m., second and fourth Saturdays of each month.

### Detroit Pediatric Society

President: Dr. Edward A. Wishropp, 10 Peterboro St., Detroit.
Secretary: Dr. W. J. Scott, 5140 Second Ave., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month from October to June, inclusive.

### Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. Joseph Yampolsky, 478 Peachtree St., Atlanta.
Secretary: Dr. T. I. Willingham, 384 Peachtree St., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

### Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. H. W. Brayton, 179 Allyn St., Hartford.
Secretary: Dr. Ernest Caulfield, 683 Asylum Ave., Hartford.

### Houston Pediatric Society

President: Dr. Walter F. Qualtrough, 920 Westheimer Ave., Houston, Texas.
Secretary-Treasurer: Dr. Allan Bloxsom, 4402 Travis St., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

### Intermountain Pediatric Society

President: Dr. Eugene Smith, 385 Twenty-Fourth St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 837 Boston Bldg., Salt Lake City, Utah.
Place: Salt Lake City, General Hospital. Time: First Thursday of each month, 8 p. m.

### Kansas City (Missouri) Pediatric Society

President: Dr. W. R. Moore, 620 Francis St., St. Joseph.
Secretary: Dr. F. S. Hogue, 1103 Grand Ave., Kansas City.
Place: Kansas City General Hospital. Time: On call.

### Los Angeles County Medical Association, Pediatric Section

President: Dr. Edwin F. Patton, 3875 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. Henry F. Gallagher, 1930 Wilshire Blvd., Los Angeles.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd.
Time: Second Monday of February, April, June, October and December.

### Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Harry Apfel, 988 Park Pl., Brooklyn.
Secretary: Dr. Max Palinsky, 1270, 45th St., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: Third Wednesday of each month, October to May.

### Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. W. C. A. Steffen, 42 Union St., Flushing, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144, 38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

### Memphis Pediatric Society

President: Dr. W. D. Mims, 1042 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. W. R. Graves, 1193 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month, except June, July and August, 8 p. m.

### Milwaukee Pediatric Society

President: Dr. George F. Kelly, 425 E. Wisconsin St., Milwaukee.
Secretary: Dr. Helen Jane Zillmer, 781 N. Jefferson St., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

### New England Pediatric Society

President: Dr. Paul Emerson, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. Henry E. Gallup, 66 Commonwealth Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

### New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Alexander T. Martin, 107 E. 85th St., New York.
Secretary: Dr. Philip M. Stimson, 25 Claremont Ave., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

### Northwestern Pediatric Society

President: Dr. A. V. Stoesser, University Hospital, Minneapolis.
Secretary: Dr. Roger L. J. Kennedy, Mayo Clinic, Rochester, Minn.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

### Philadelphia Pediatric Society

President: Dr. H. H. Perlman, 1904 N. Franklin St., Philadelphia.
Secretary: Dr. James E. Bowman, 4091 Comly St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

### Pittsburgh Pediatric Society

President: Dr. James LeRoy Foster, Highland Bldg., Pittsburgh.
Secretary-Treasurer: Dr. E. R. McClusky, 3200 Fifth Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

### Richmond Pediatric Society

President: Dr. Lee E. Sutton, Jr., 2601 Grove Ave., Richmond, Va.
Secretary-Treasurer: Dr. Louise Fry Galvin, 2416 Stuart Ave., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

### Rochester Pediatric Society

President: Dr. F. W. Bush, 29 N. Goodman St., Rochester, N. Y.
Secretary: Dr. David Wolin, 16 N. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month.

### Rocky Mountain Pediatric Society

President: Dr. James E. Russell Jr., 820 Metropolitan Bldg., Denver.
Secretary: Dr. F. Craig Johnson, 1850 Gilpin St., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 2:30 p. m.

### St. Louis Pediatric Society

President: Dr. John Zahorsky, 536 N. Taylor Ave., St. Louis.
Secretary-Treasurer: Dr. Max Deutch, 634 N. Grand Blvd., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

### Seattle Pediatric Society

President: Dr. Frank H. Douglass, Medical Dental Bldg., Seattle.
Secretary: Dr. C. Lu Verne Smith, Stimson Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

### Southwestern Pediatric Society

President: Dr. Howard R. Cooder, 3875 Wilshire Blvd., Los Angeles.
Secretary: Dr. Philip E. Rothman, 3875 Wilshire Blvd., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May September and November.

### University of Michigan Pediatric and Infectious Disease Society

President: Dr. M. Cooperstock, Northern Michigan Children's Clinic, Marquette.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.

### Westchester County Medical Society, Pediatric Section (New York)

President: Dr. Louis V. Waldron, 149 N. Broadway, Yonkers, N. Y.
Secretary-Treasurer: Dr. Fairfax Hall, 421 Huguenot St., New Rochelle, N. Y.
Place: Grasslands Hospital. Time: Third Thursday, October, December, February and April.